=> b reg
FILE 'REGISTRY' ENTERED AT 09:45:05 ON 30 MAR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 29 MAR 2004 HIGHEST RN 668968-88-5
DICTIONARY FILE UPDATES: 29 MAR 2004 HIGHEST RN 668968-88-5

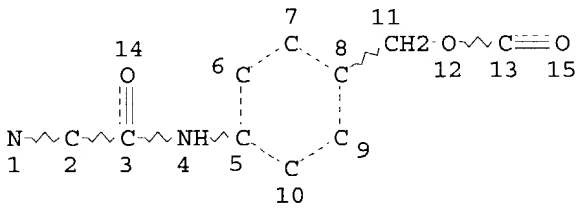
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que l3
L1 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
L3 219 SEA FILE=REGISTRY SSS FUL L1

=> b hcaplus
FILE 'HCAPLUS' ENTERED AT 09:45:32 ON 30 MAR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 30 Mar 2004 VOL 140 ISS 14
FILE LAST UPDATED: 29 Mar 2004 (20040329/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que l9 nos

L1		STR	
L3	219	SEA FILE=REGISTRY SSS FUL L1	
L4	32	SEA FILE=HCAPLUS ABB=ON PLU=ON	L3
L5	21062	SEA FILE=HCAPLUS ABB=ON PLU=ON	DEXTRAN?/OBI OR CARBOXYMETHYLD EXTRAN?/OBI OR POLYALCOHOL?/OBI
L6	3	SEA FILE=HCAPLUS ABB=ON PLU=ON	L4 AND L5
L7	212287	SEA FILE=HCAPLUS ABB=ON PLU=ON	CONJUGAT?/OBI OR CARRIER?/OBI
L8	12	SEA FILE=HCAPLUS ABB=ON PLU=ON	L7 AND L4
L9	12	SEA FILE=HCAPLUS ABB=ON PLU=ON	L8 OR L6

=> d ibib abs hitstr l9 1-12

L9 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:651761 HCAPLUS
DOCUMENT NUMBER: 140:92253
TITLE: cAC10-vcMMAE, an anti-CD30-monomethyl auristatin E **conjugate** with potent and selective antitumor activity
AUTHOR(S): Francisco, Joseph A.; Cerveny, Charles G.; Meyer, Damon L.; Mixan, Bruce J.; Klussman, Kerry; Chace, Dana F.; Rejniak, Starr X.; Gordon, Kristine A.; DeBlanc, Ron; Toki, Brian E.; Law, Che-Leung; Doronina, Svetlana O.; Siegall, Clay B.; Senter, Peter D.; Wahl, Alan F.
CORPORATE SOURCE: Seattle Genetics, Bothell, WA, 98021, USA
SOURCE: Blood (2003), 102(4), 1458-1465
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The chimeric monoclonal antibody cAC10, directed against CD30, induces growth arrest of CD30+ cell lines in vitro and has pronounced antitumor activity in severe combined immunodeficiency (SCID) mouse xenograft models of Hodgkin disease. We have significantly enhanced these activities by conjugating to cAC10 the cytotoxic agent monomethyl auristatin E (MMAE) to create the antibody-drug conjugate cAC10-vcMMAE. MMAE, a derivative of the cytotoxic tubulin modifier auristatin E, was covalently coupled to cAC10 through a valine-citrulline peptide linker. The drug was stably attached to the antibody, showing only a 2% release of MMAE following 10-day incubation in human plasma, but it was readily cleaved by lysosomal proteases after receptor-mediated internalization. Release of MMAE into the cytosol induced G2/M-phase growth arrest and cell death through the induction of apoptosis. In vitro, cAC10-vcMMAE was highly potent and selective against CD30+ tumor lines (IC50 less than 10 ng/mL) but was more than 300-fold less active on antigen-neg. cells. In SCID mouse xenograft

models of anaplastic large cell lymphoma or Hodgkin disease, cAC10-vcMMAE was efficacious at doses as low as 1 mg/kg. Mice treated at 30 mg/kg cAC10-vcMMAE showed no signs of toxicity. These data indicate that cAC10-vcMMAE may be a highly effective and selective therapy for the treatment of CD30+ neoplasias.

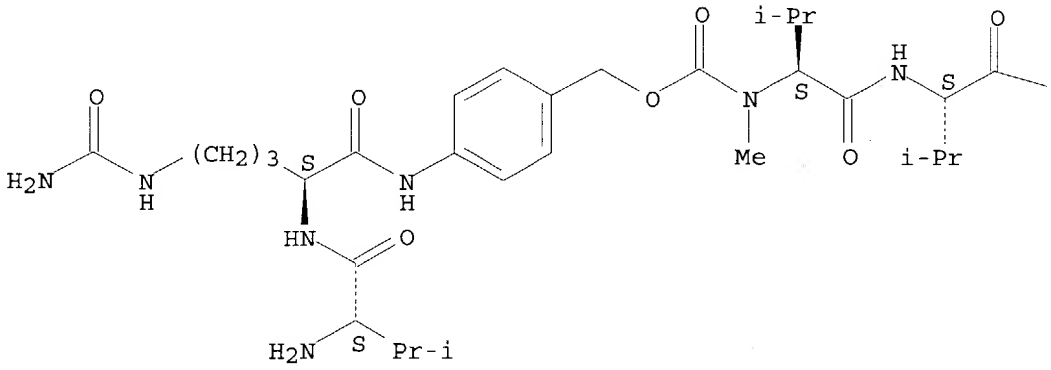
IT **644981-35-1D**, antibody **conjugates**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cAC10-vcMMAE, an anti-CD30-monomethyl auristatin E **conjugate** with potent and selective antitumor activity)

RN 644981-35-1 HCAPLUS

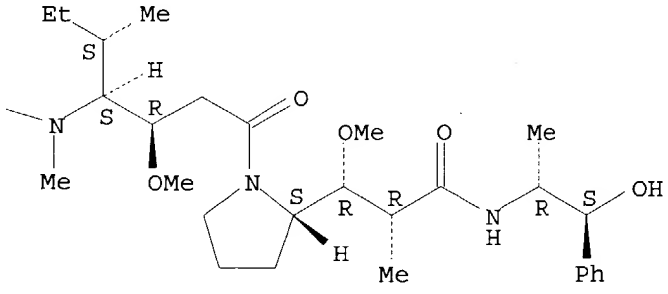
CN L-Valinamide, N-methyl-N-[[[4-[[L-valyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]-L-valyl-N-[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[(1R,2S)-2-hydroxy-1-methyl-2-phenylethyl]amino]-1-methoxy-2-methyl-3-oxopropyl]-1-pyrrolidinyl]-2-methoxy-1-[(1S)-1-methylpropyl]-4-oxobutyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:532329 HCAPLUS
DOCUMENT NUMBER: 139:106453
TITLE: p-Amidobenzyl ethers of drugs in drug delivery systems

INVENTOR(S): Senter, Peter D.; Toki, Brian E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of U.S. Ser. No. 963,103.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003130189	A1	20030710	US 2002-252947	20020923
US 2003096743	A1	20030522	US 2001-963103	20010924
WO 2003026577	A2	20030403	WO 2002-US30282	20020924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

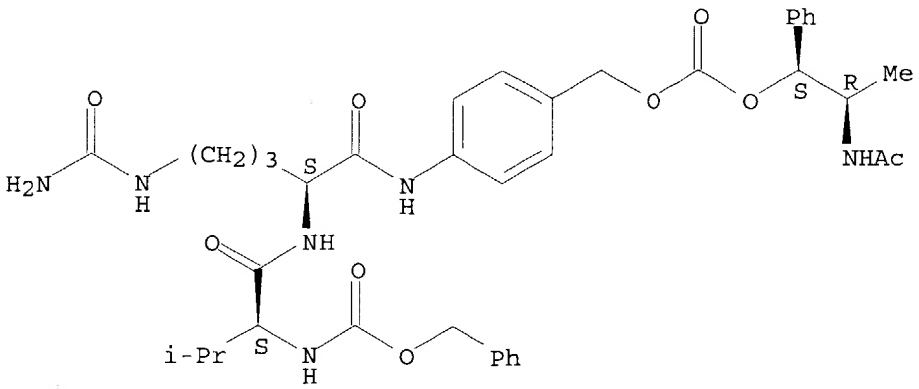
PRIORITY APPLN. INFO.: US 2001-963103 A2 20010924
US 2002-252947 A 20020923
OTHER SOURCE(S): MARPAT 139:106453

AB Compns. containing conjugates containing a drug moiety, a ligand and an optional acyl unit, an amino acid or a peptide, an aminobenzyl ether self-immolative spacer group, an optional second self-immolative group, and carriers, diluents and/or excipients, and methods of delivery the drug are described. Thus, a peptide was treated with 1-naphthol to give a derivative The compound was very stable in human serum, and showed antitumor activity.

IT **410093-13-9P 410093-14-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amidobenzyl ethers of drugs in drug delivery systems)

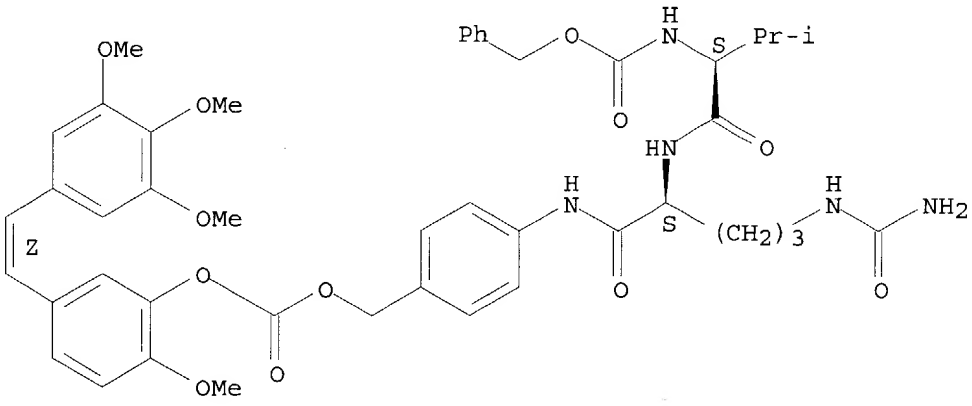
RN 410093-13-9 HCAPLUS
CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N-[4-[[[[(1S,2R)-2-(acetylamino)-1-phenylpropoxy]carbonyl]oxy]methyl]phenyl]-N5-(aminocarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 410093-14-0 HCAPLUS
CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N5-(aminocarbonyl)-N-[4-[[[[2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]phenoxy]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L9 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:493869 HCAPLUS
DOCUMENT NUMBER: 140:117183
TITLE: Development of potent monoclonal antibody auristatin **conjugates** for cancer therapy
AUTHOR(S): Doronina, Svetlana O.; Toki, Brian E.; Torgov, Michael Y.; Mendelsohn, Brian A.; Cerveny, Charles G.; Chace, Dana F.; DeBlanc, Ron L.; Gearing, R. Patrick; Bovee, Tim D.; Siegall, Clay B.; Francisco, Joseph A.; Wahl, Alan F.; Meyer, Damon L.; Senter, Peter D.
CORPORATE SOURCE: Seattle Genetics, Inc., Bothell, WA, 98021, USA
SOURCE: Nature Biotechnology (2003), 21(7), 778-784
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We describe the in vitro and in vivo properties of monoclonal antibody (mAb)-drug conjugates consisting of the potent synthetic dolastatin 10

analogs auristatin E (AE) and monomethylauristatin E (MMAE), linked to the chimeric mAbs cBR96 (specific to Lewis Y on carcinomas) and cAC10 (specific to CD30 on hematol. malignancies). The linkers used for conjugate formation included an acid-labile hydrazone and protease-sensitive dipeptides, leading to uniformly substituted conjugates that efficiently released active drug in the lysosomes of antigen-pos. (Ag+) tumor cells. The peptide-linked mAb-valine-citrulline-MMAE and mAb-phenylalanine-lysine-MMAE conjugates were much more stable in buffers and plasma than the conjugates of mAb and the hydrazone of 5-benzoylvaleric acid-AE ester (AEVB). As a result, the mAb-Val-Cit-MMAE conjugates exhibited greater in vitro specificity and lower in vivo toxicity than corresponding hydrazone conjugates. In vivo studies demonstrated that the peptide-linked conjugates induced regressions and cures of established tumor xenografts with therapeutic indexes as high as 60-fold. These conjugates illustrate the importance of linker technol., drug potency and conjugation methodol. in developing safe and efficacious mAb-drug conjugates for cancer therapy.

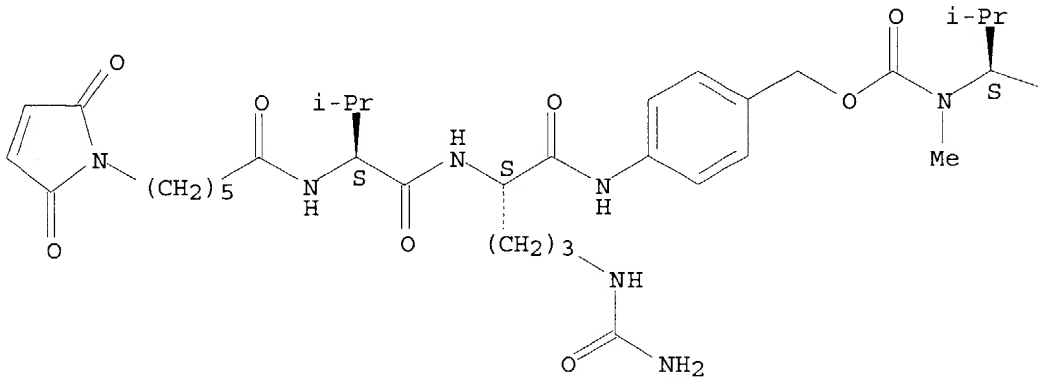
IT **646502-53-6DP, conjugates** with monoclonal antibody
646502-54-7DP, conjugates with monoclonal antibody
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(development of potent monoclonal antibody-auristatin **conjugates** for cancer therapy)

RN 646502-53-6 HCAPLUS

CN L-Valinamide, N-[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-valyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]-N-methyl-L-valyl-N-[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[(1R,2S)-2-hydroxy-1-methyl-2-phenylethyl]amino]-1-methoxy-2-methyl-3-oxopropyl]-1-pyrrolidinyl]-2-methoxy-1-[(1S)-1-methylpropyl]-4-oxobutyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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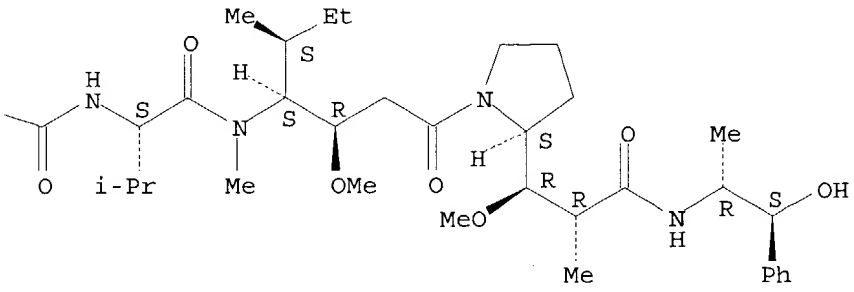
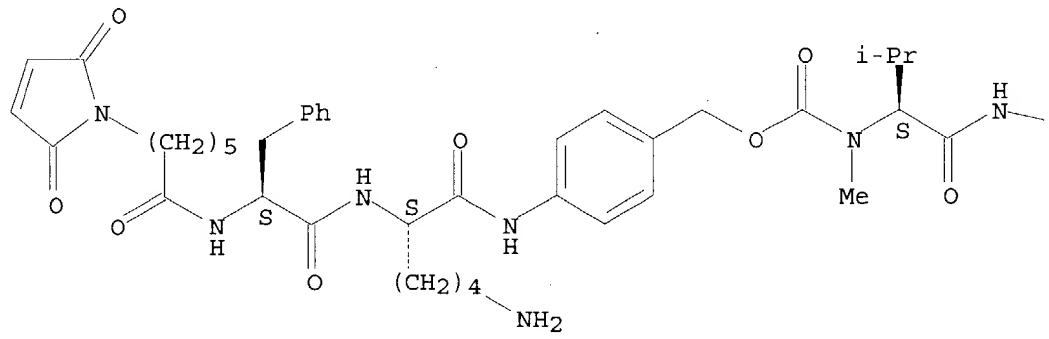


RN 646502-54-7 HCAPLUS

CN L-Valinamide, N-[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]-N-methyl-L-valyl-N-[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[(1R,2S)-2-hydroxy-1-methyl-2-phenylethyl]amino]-1-methoxy-2-methyl-3-oxopropyl]-1-pyrrolidinyl]-2-methoxy-1-[(1S)-1-methylpropyl]-4-oxobutyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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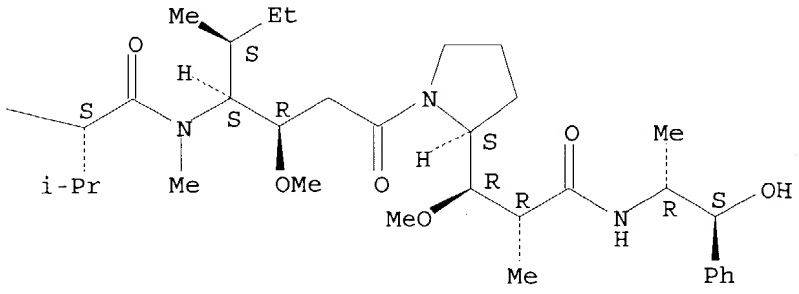


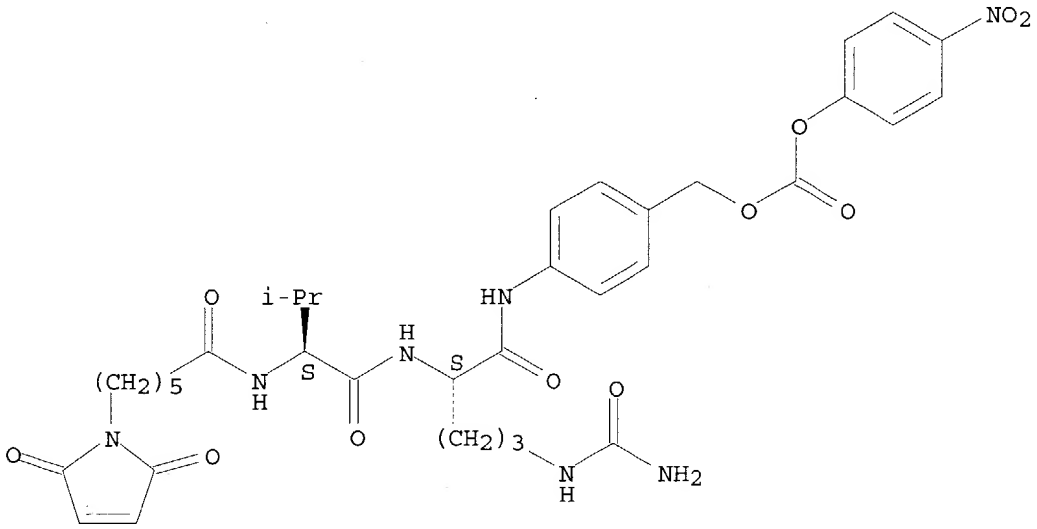
IT **159857-81-5 646502-56-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(development of potent monoclonal antibody-auristatin

conjugates for cancer therapy)

RN 159857-81-5 HCAPLUS

CN L-Ornithinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-valyl-N5-(aminocarbonyl)-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

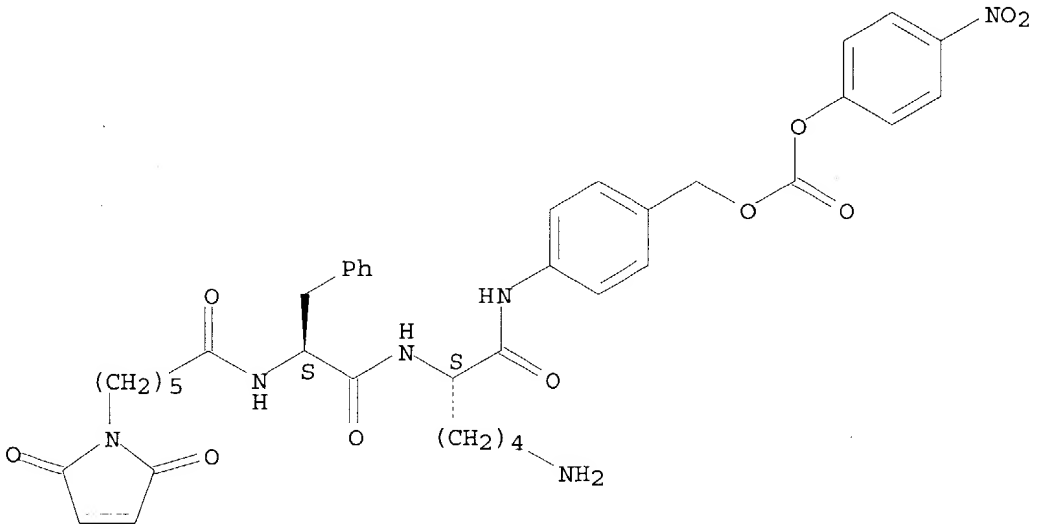
Absolute stereochemistry.



RN 646502-56-9 HCAPLUS

CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **646502-53-6P 646502-54-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

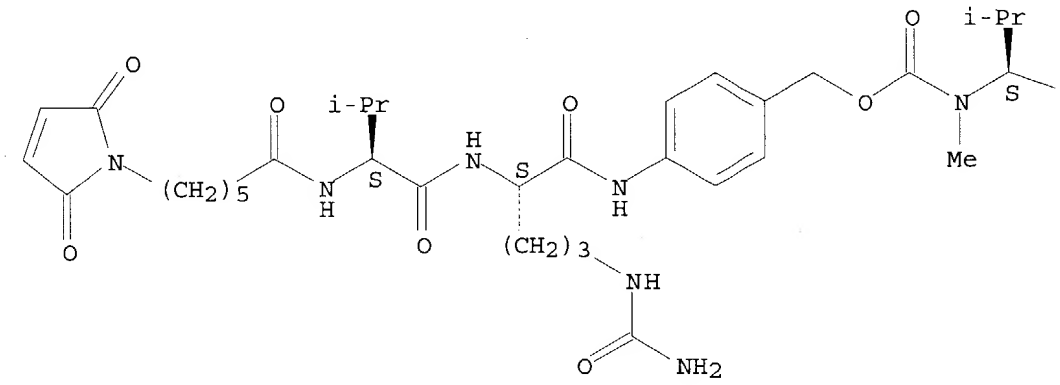
(development of potent monoclonal antibody-auristatin **conjugates** for cancer therapy)

RN 646502-53-6 HCAPLUS

CN L-Valinamide, N-[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-valyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]-N-methyl-L-valyl-N-[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[(1R,2S)-2-hydroxy-1-methyl-2-phenylethyl]amino]-1-methoxy-2-methyl-3-oxopropyl]-1-pyrrolidinyl]-2-methoxy-1-[(1S)-1-methylpropyl]-4-oxobutyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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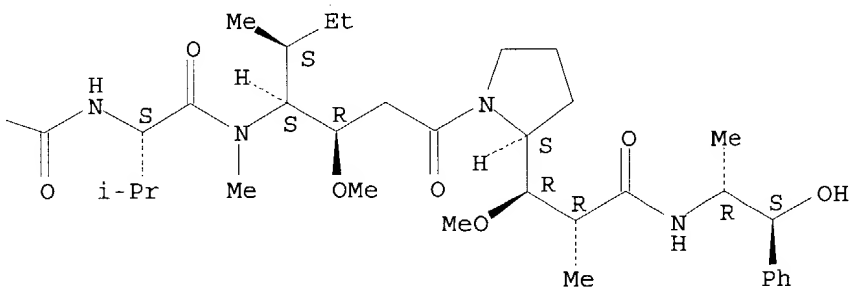
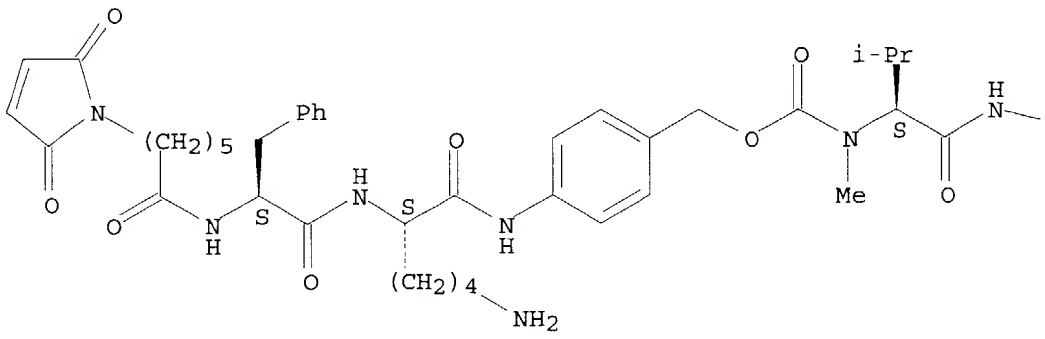


RN 646502-54-7 HCAPLUS

CN L-Valinamide, N-[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]-N-methyl-L-valyl-N-[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[(1R,2S)-2-hydroxy-1-methyl-2-phenylethyl]amino]-1-methoxy-2-methyl-3-oxopropyl]-1-pyrrolidinyl]-2-methoxy-1-[(1S)-1-methylpropyl]-4-oxobutyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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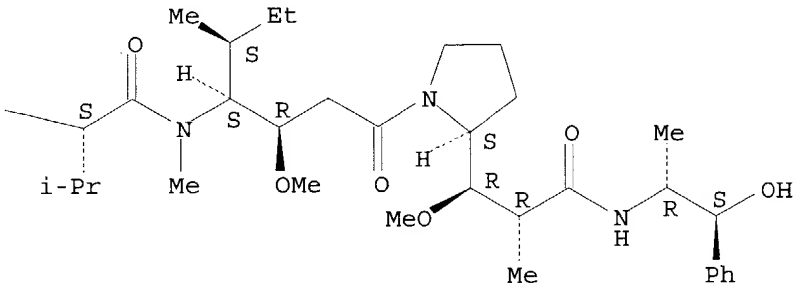


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:261611 HCAPLUS
DOCUMENT NUMBER: 138:292740
TITLE: p-Amidobenzyl ethers in drug delivery agents
INVENTOR(S): Senter, Peter D.; Toki, Brian E.
PATENT ASSIGNEE(S): Seattle Genetics, Inc., USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026577	A2	20030403	WO 2002-US30282	20020924

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003096743	A1	20030522	US 2001-963103		20010924
US 2003130189	A1	20030710	US 2002-252947		20020923

PRIORITY APPLN. INFO.: US 2001-963103 A 20010924
US 2002-252947 A 20020923

OTHER SOURCE(S): MARPAT 138:292740

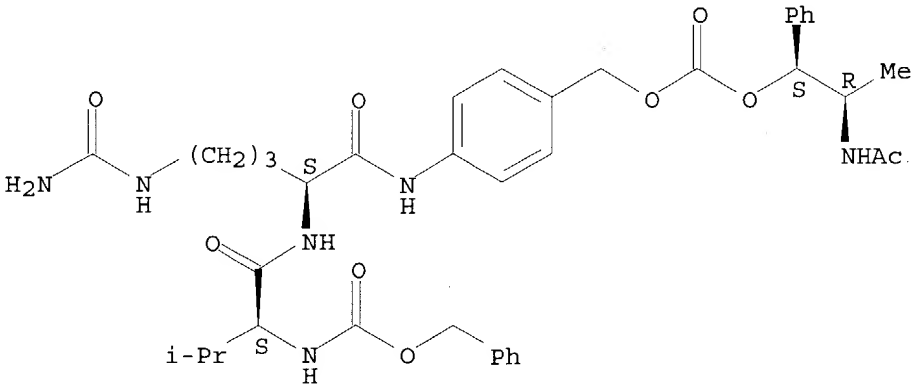
AB Compds. [L-[-An-Z-X-Ww-]-D and B-[-Z-X-Ww-]-D, where D is a drug moiety, L is a ligand, B is a blocking group, A = acyl Z = amino acid or a peptide, X = aminobenzyl ether spacer group, W = optional second group, n = 0 or 1, and w = 0 or 1] and compns. of the compds. with carriers, diluents and/or excipients, and methods of delivery of the drugs are disclosed. Thus, etoposide was allowed to react with a peptide-containing and the product obtained was shown to be very stable at pH 5.1 and 7.2 after 7 days.

IT **410093-13-9P 410093-14-0P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amidobenzyl ethers as drug delivery agents)

RN 410093-13-9 HCAPLUS

CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N-[4-[[[[(1S,2R)-2-(acetylamino)-1-phenylpropoxy]carbonyl]oxy]methyl]phenyl]-N5-(aminocarbonyl)- (9CI) (CA INDEX NAME)

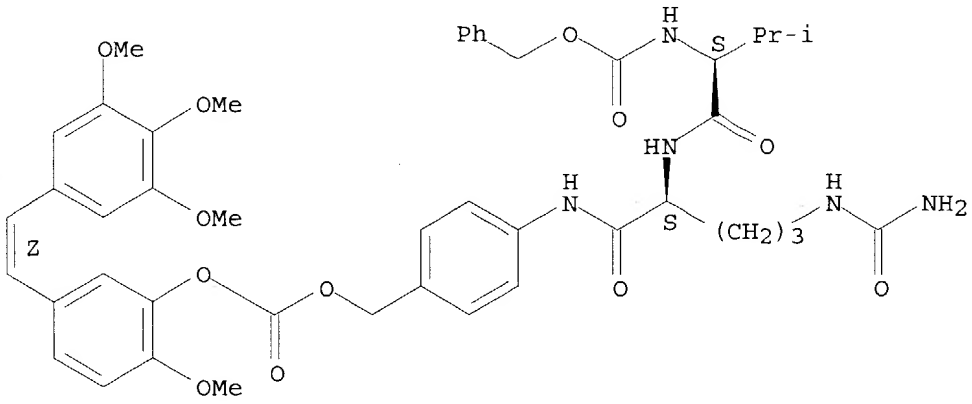
Absolute stereochemistry.



RN 410093-14-0 HCAPLUS

CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N5-(aminocarbonyl)-N-[4-[[[[2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]phenoxy]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L9 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:604475 HCAPLUS
DOCUMENT NUMBER: 137:288653
TITLE: Monoclonal Antibody **Conjugates** of Doxorubicin Prepared with Branched Peptide Linkers: Inhibition of Aggregation by Methoxytriethyleneglycol Chains
AUTHOR(S): King, H. Dalton; Dubowchik, Gene M.; Mastalerz, Harold; Willner, David; Hofstead, Sandra J.; Firestone, Raymond A.; Lasch, Shirley J.; Trail, Pamela A.
CORPORATE SOURCE: Bristol Myers Squibb Pharmaceutical Research Institute, Wallingford, NJ, 08543, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(19), 4336-4343
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB High mole ratio BR96 immunoconjugates were synthesized using branched peptide-doxorubicin linkers designed to liberate doxorubicin following antigen-specific internalization into lysosomes. However, these immunoconjugates are highly prone to noncovalent, dimeric aggregation. We hypothesize that this is due to (1) the hydrophobic nature of the peptides, (2) the loss of pos. charge upon amide formation at the 3'-amino group of doxorubicin, and (3) the proximity of the peptide hydrophobic residues to form efficient intermol. stacking interactions. By introducing a hydrophilic methoxytriethylene glycol chain onto the doxorubicin portion of the branched peptide linkers, aggregation has been eliminated or greatly reduced in the immunoconjugate products. The methoxytriethylene glycol chain was linked to the doxorubicin moiety of the linker via a hydrazone bond that is stable at pH 7 but hydrolyzes rapidly at pH 5 to release free drug. BR96 immunoconjugates synthesized from methoxytriethylene glycol-modified branched peptide-doxorubicin linkers are highly potent and immunospecific in vitro. The data suggest that the methoxytriethylene glycol chain hydrolyzes as designed upon antigen-specific internalization into tumor lysosomes in vitro, where enzymic degradation of the peptide linker releases free doxorubicin.

IT **159857-68-8DP**, **conjugates** with IgG1 BR96
207613-83-0DP, **conjugates** with IgG1 BR96
469888-00-4DP, **conjugate** with IgG1 BR96
469888-01-5DP, **conjugate** with IgG1 BR96

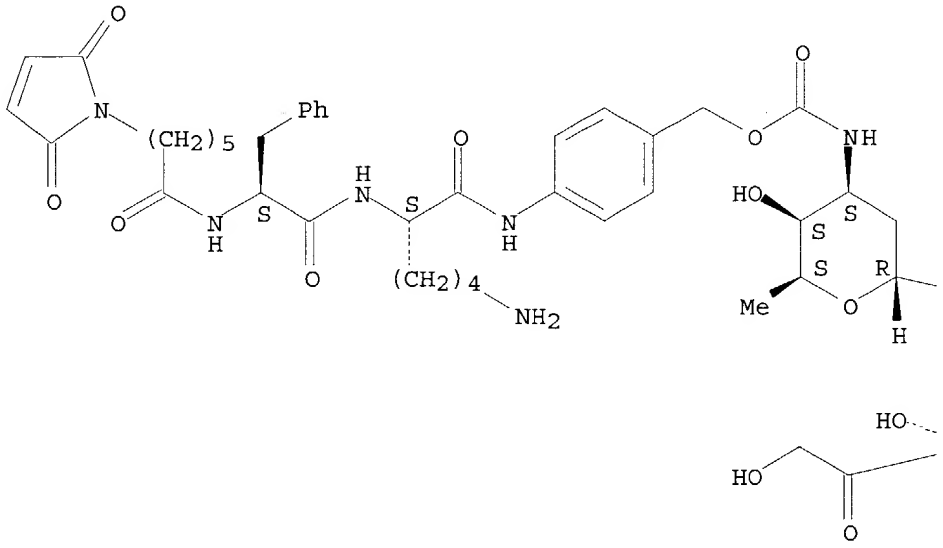
469888-04-8DP, conjugates with IgG1 BR96
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MAb **conjugates** of doxorubicin prepared with branched peptide linkers: aggregation inhibition by methoxytriethyleneglycol chains and cytototoxicity against lung cancer)

RN 159857-68-8 HCAPLUS

CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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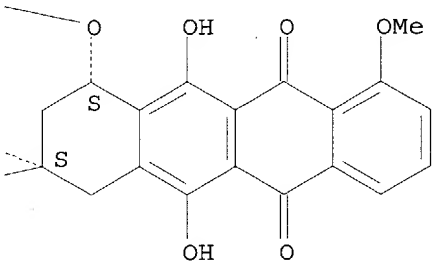
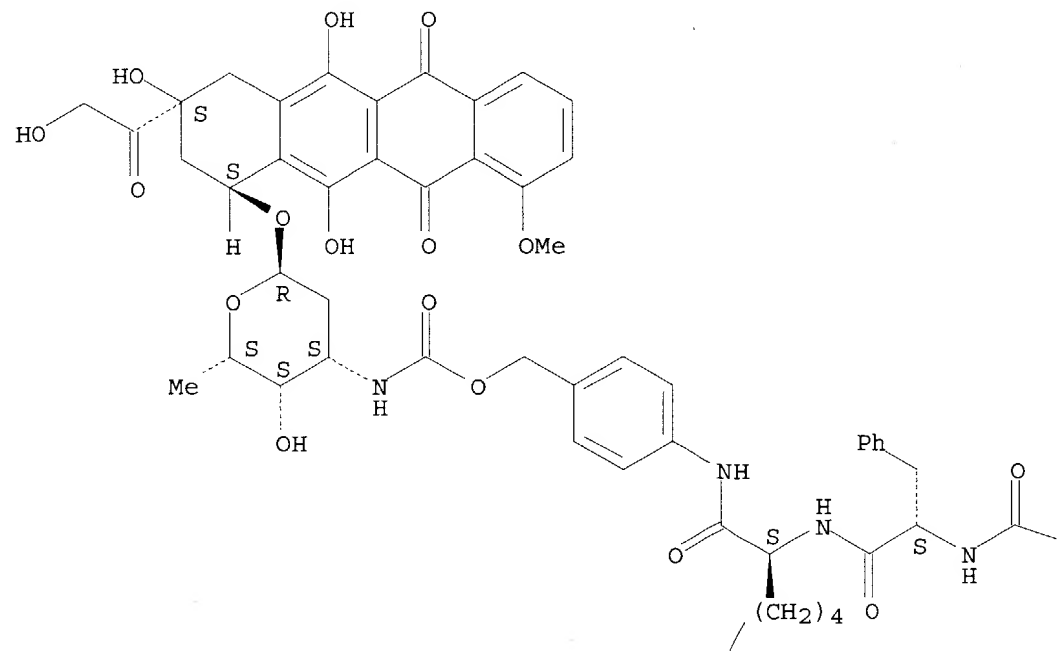


RN 207613-83-0 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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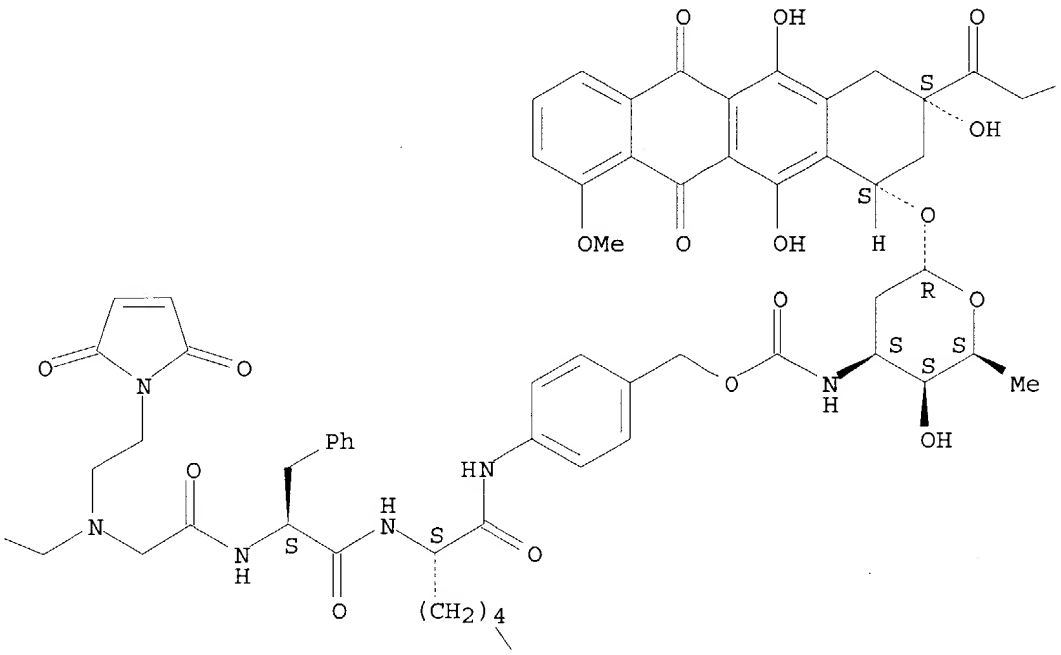


Searched by P. Ruppel

PAGE 1-C

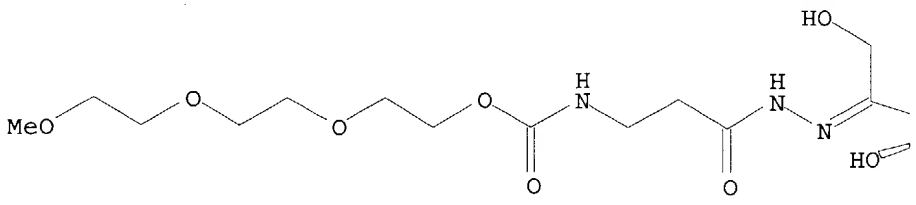
PAGE 2-A

PAGE 2-B

RN 469888-00-4 HCAPLUS
CN 2,5,8,11-Tetraoxa-13-azahexadecan-16-oic acid, 12-oxo-, [1-[(2S,4S)-4-[[3-[[[[4-[[N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide, (1'→1''')-amide with 12-oxo-2,5,8,11-tetraoxa-13-azahexadecan-16-oic acid [1-[(2S,4S)-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-4-[[2,3,6-trideoxy-3-[[[[4-[(L-phenylalanyl-L-lysyl)amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-2-naphthacenyl]-2-hydroxyethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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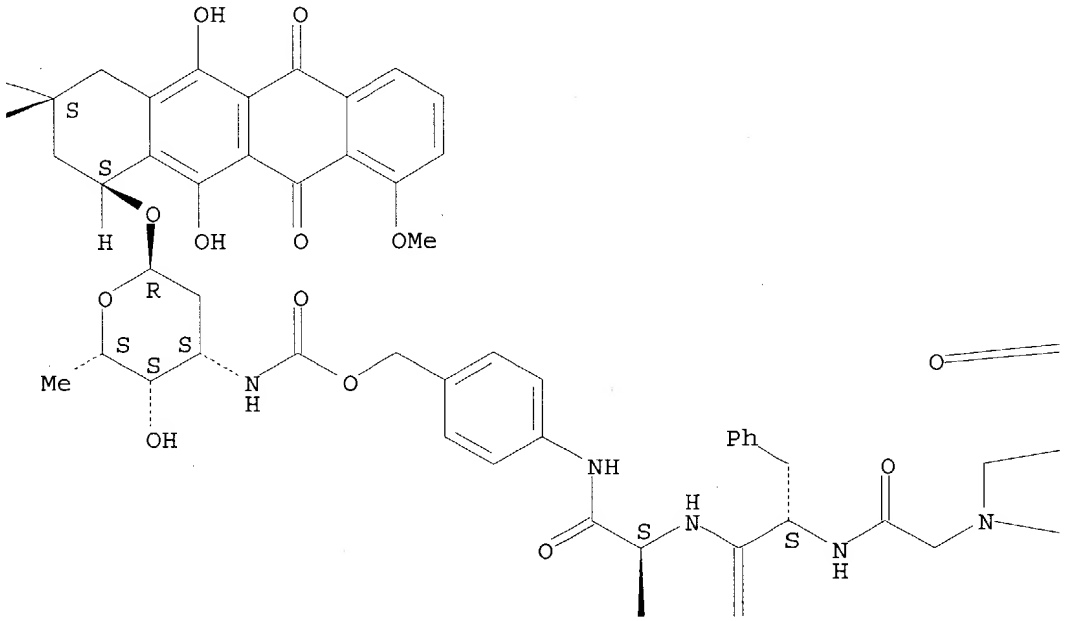

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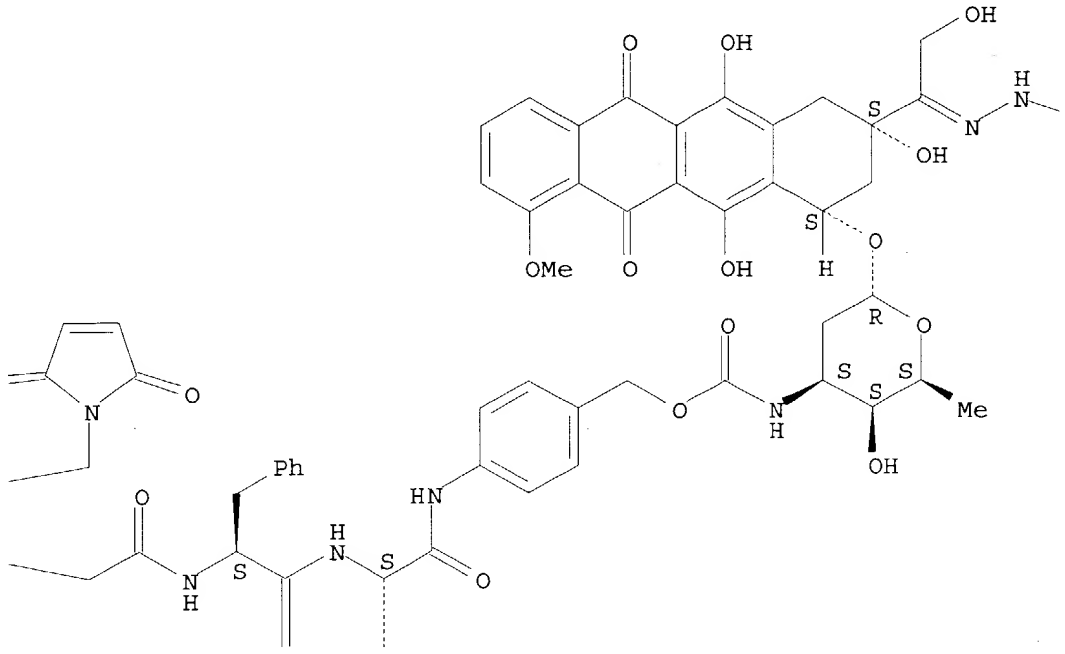

Searched by P. Ruppel

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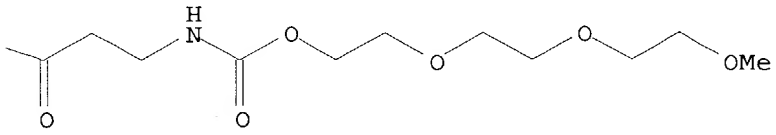

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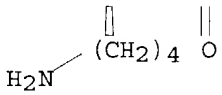

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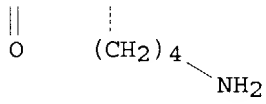

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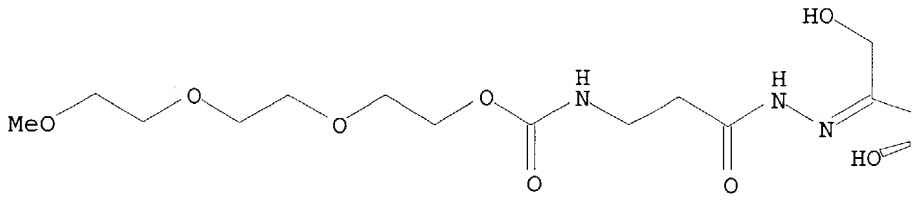
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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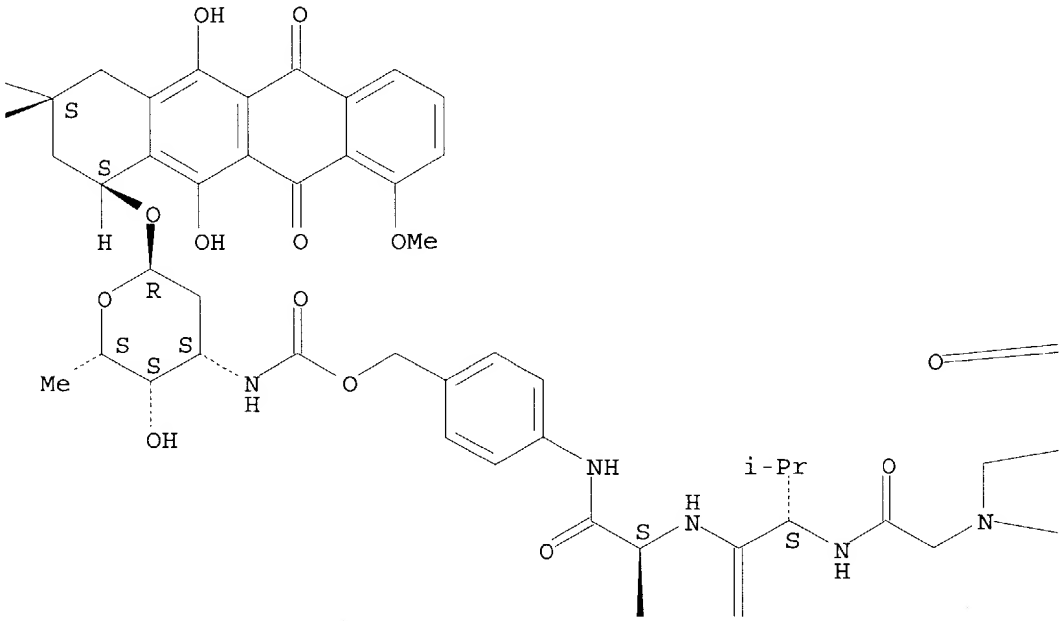

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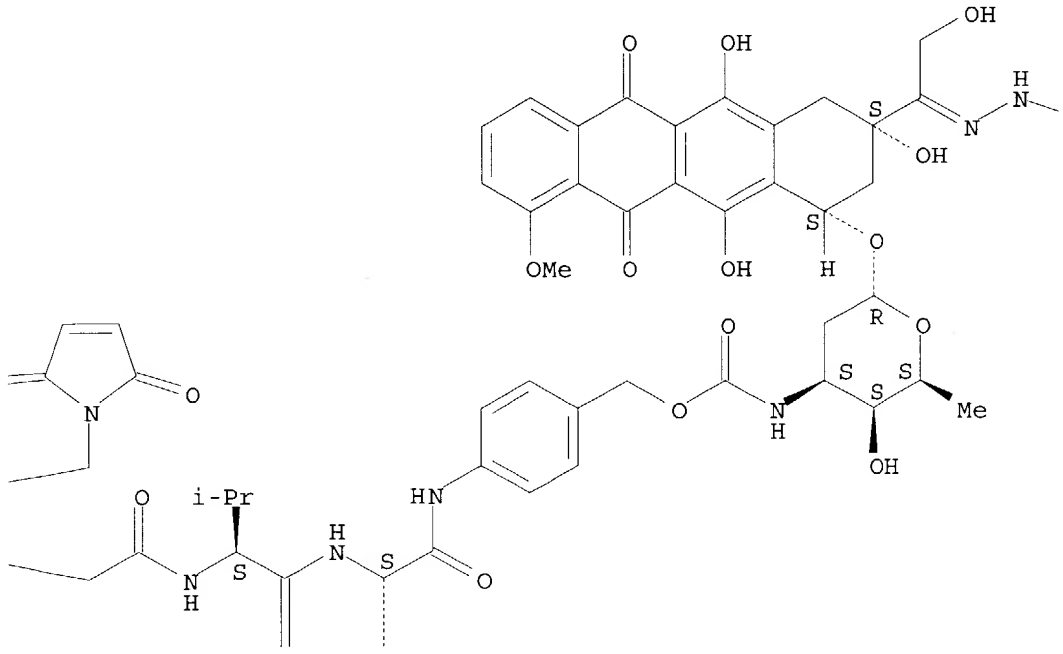

Searched by P. Ruppel

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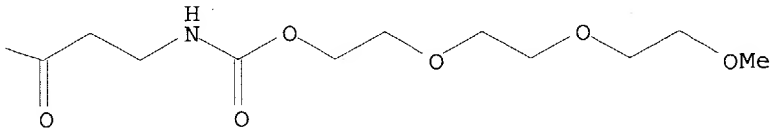

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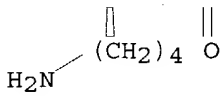

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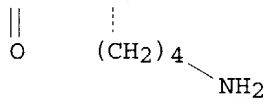
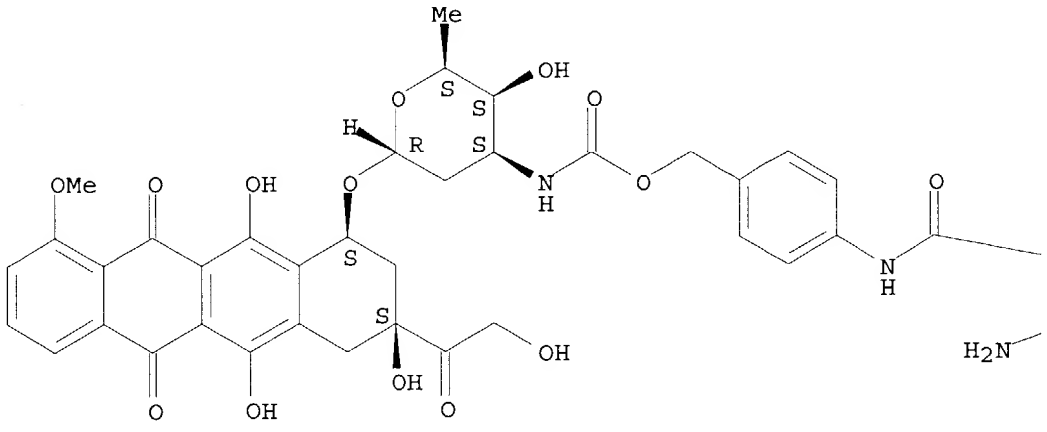


RN 469888-04-8 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-valyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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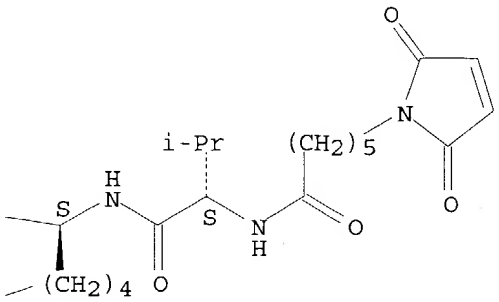


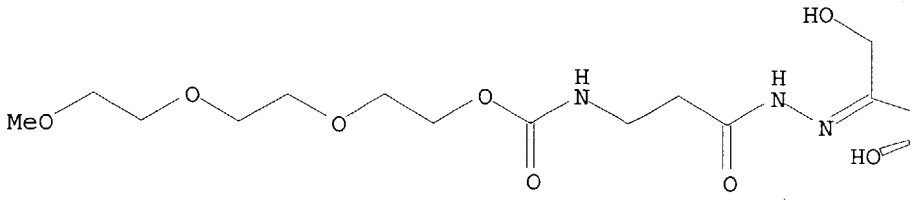
IT **469888-00-4P 469888-01-5P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(MAb **conjugates** of doxorubicin prepared with branched peptide linkers: aggregation inhibition by methoxytriethyleneglycol chains and cytototoxicity against lung cancer)

RN 469888-00-4 HCAPLUS

CN 2,5,8,11-Tetraoxa-13-azahexadecan-16-oic acid, 12-oxo-, [1-[(2S,4S)-4-[[3-[[[[4-[[N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide, (1'→1''')-amide with 12-oxo-2,5,8,11-tetraoxa-13-azahexadecan-16-oic acid [1-[(2S,4S)-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-4-[[2,3,6-trideoxy-3-[[[[4-[(L-phenylalanyl-L-lysyl)amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-2-naphthacenyl]-2-hydroxyethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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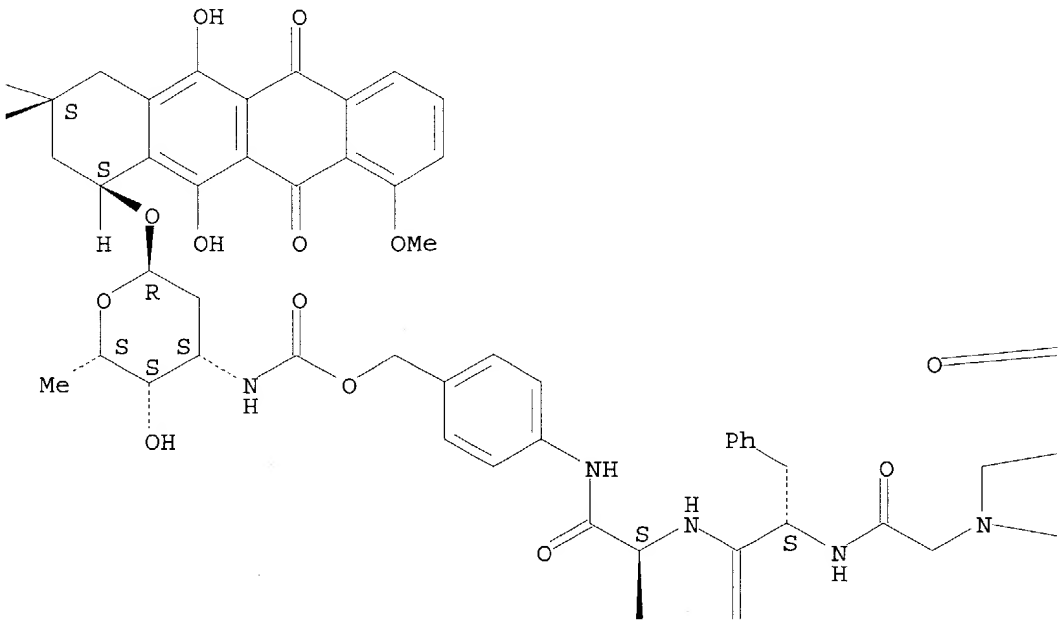

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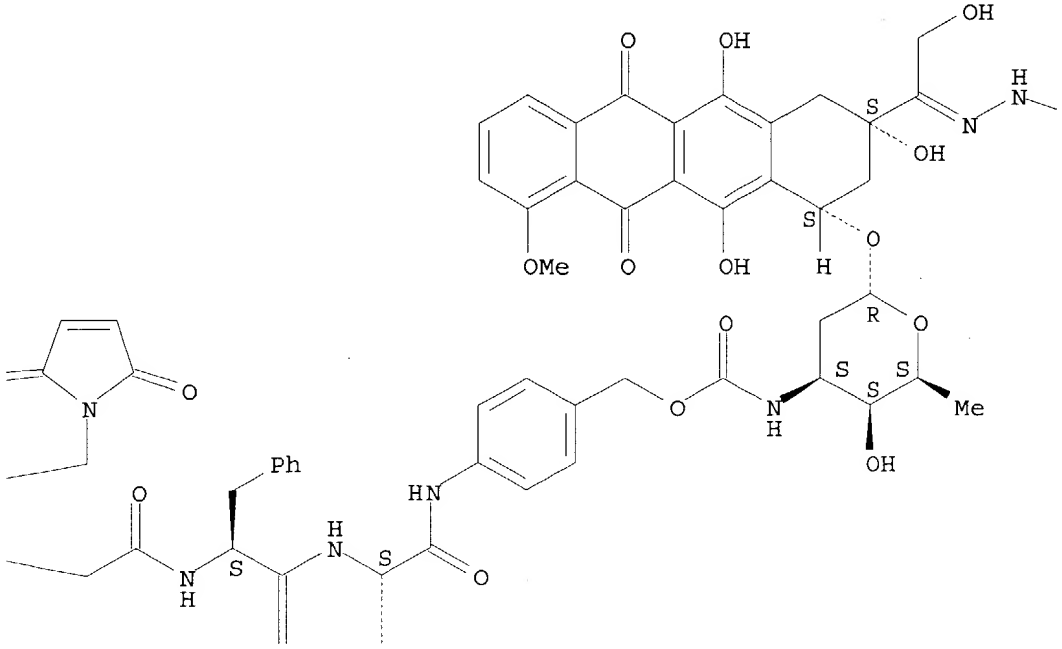

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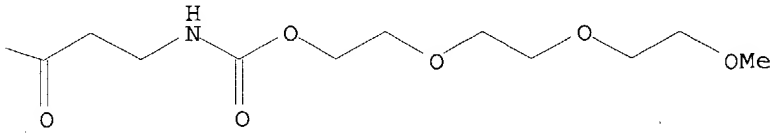

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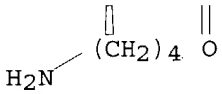

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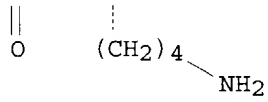

RN 469888-01-5 HCAPLUS
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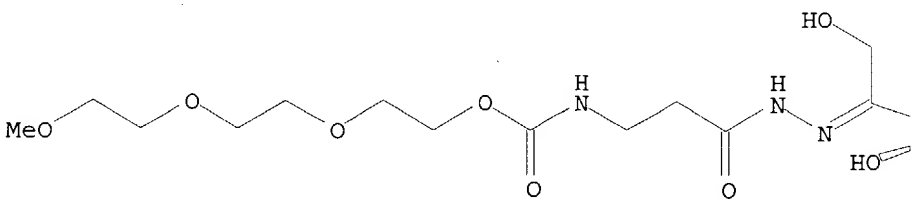
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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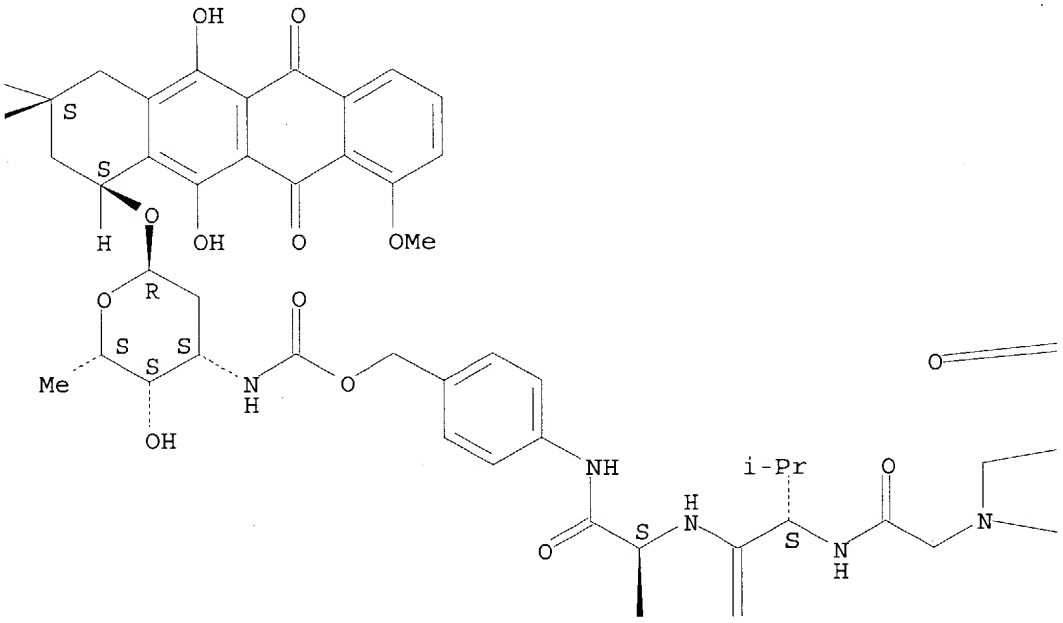

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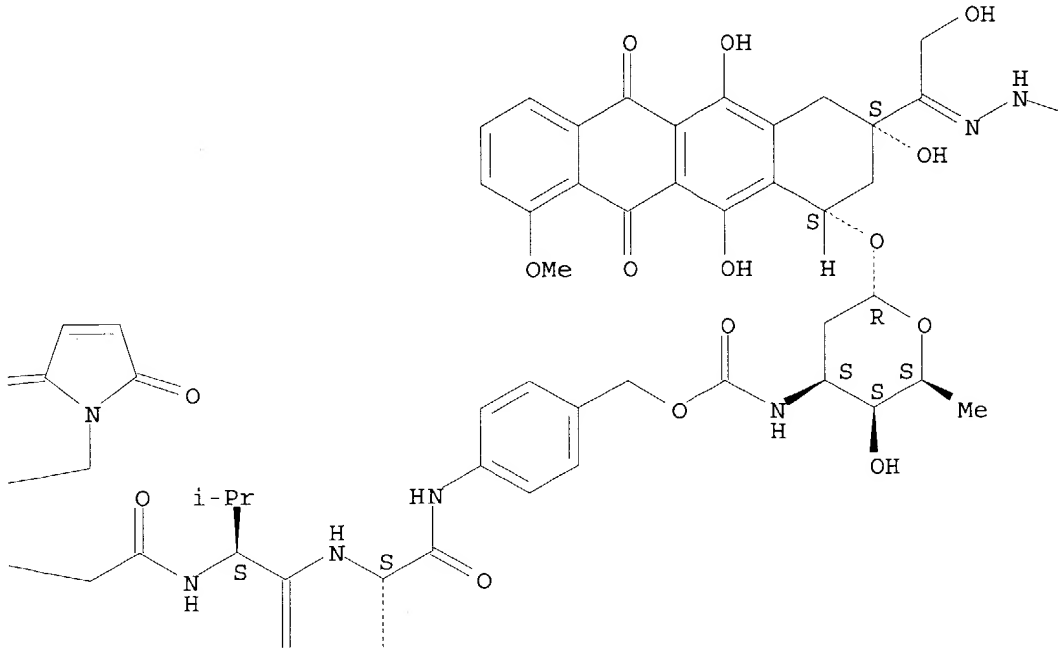

Searched by P. Ruppel

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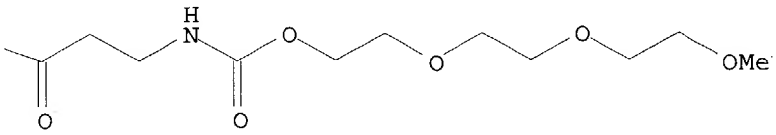

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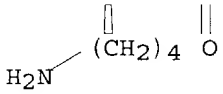

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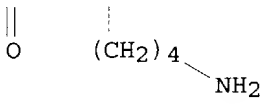


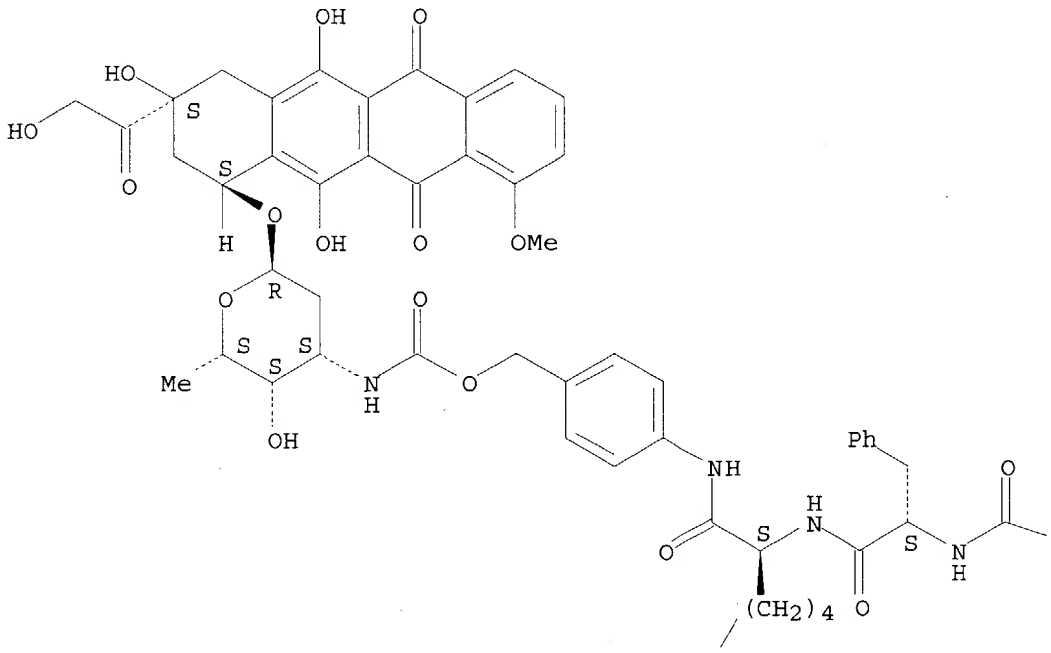
IT **207613-83-0 207613-85-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(MAb **conjugates** of doxorubicin prepared with branched peptide linkers: aggregation inhibition by methoxytriethyleneglycol chains and cytototoxicity against lung cancer)

RN 207613-83-0 HCAPLUS

CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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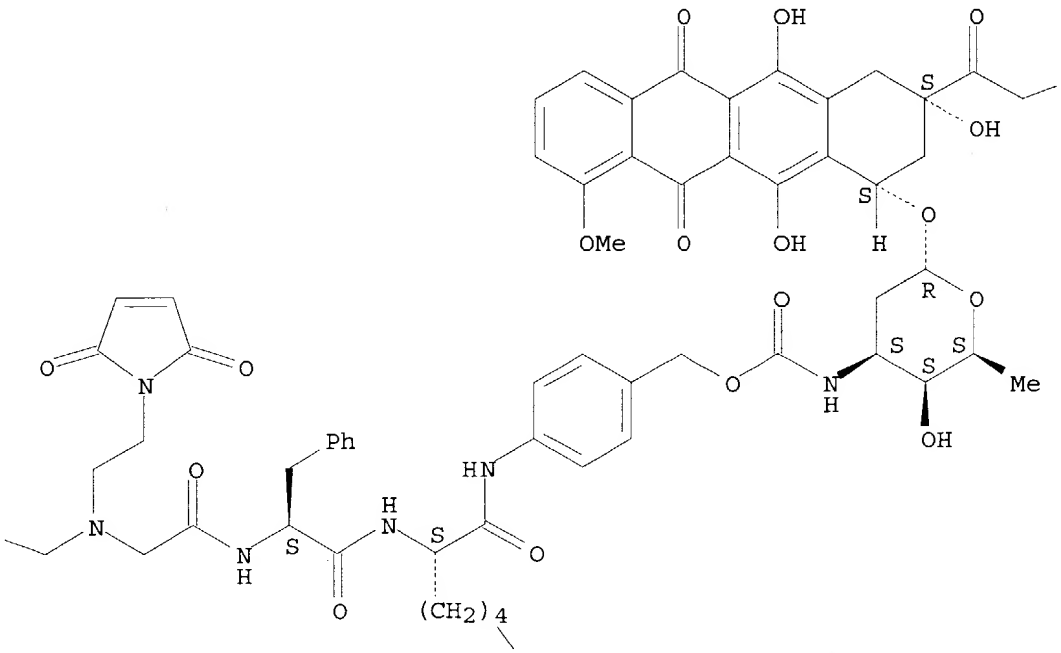


Searched by P. Ruppel

PAGE 1-C

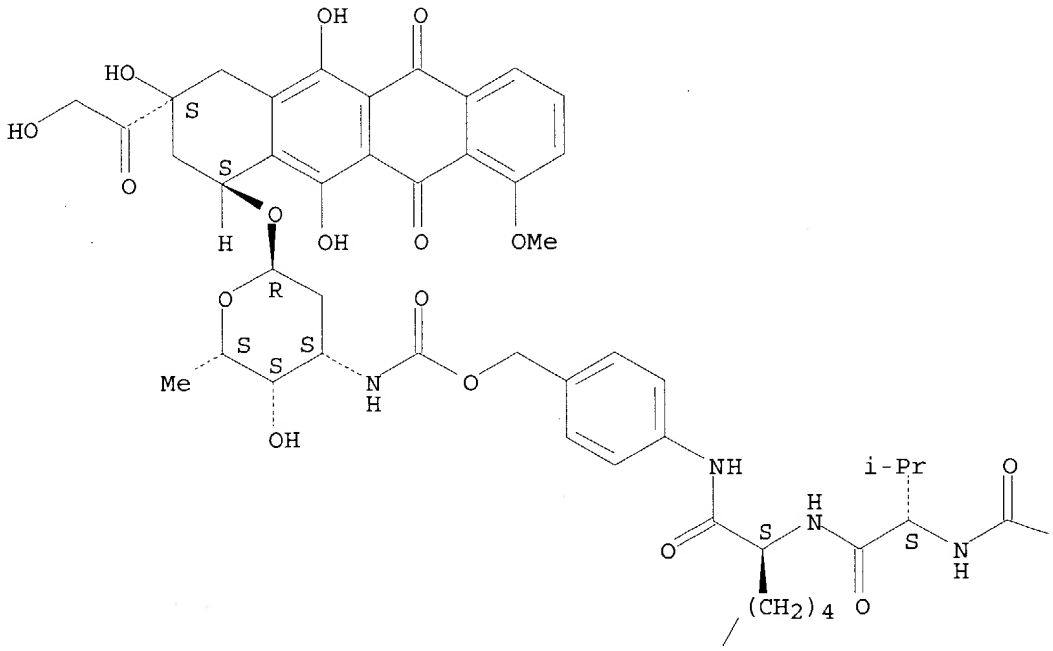
PAGE 2-A

PAGE 2-B

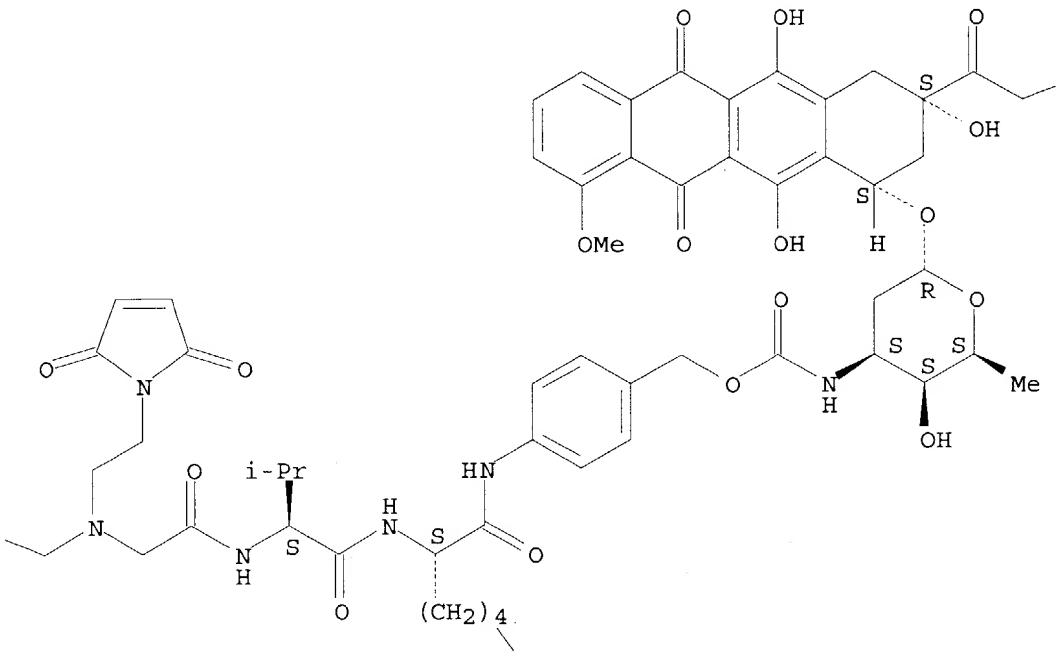
RN 207613-85-2 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-valyl-N-[4-(hydroxymethyl)phenyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-valyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



Searched by P. Ruppel

PAGE 1-C

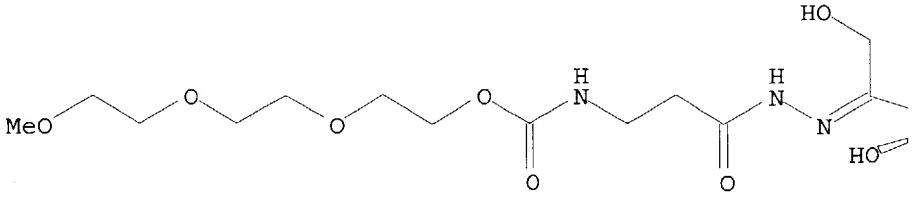
PAGE 2-A

PAGE 2-B

IT **469888-02-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(MAb **conjugates** of doxorubicin prepared with branched peptide linkers: aggregation inhibition by methoxytriethyleneglycol chains and cytototoxicity against lung cancer)
RN 469888-02-6 HCAPLUS
CN 2,5,8,11-Tetraoxa-13-azahexadecan-16-oic acid, 12-oxo-, [1-[(2S,4S)-4-[[3-[[[[4-[[N-(carboxymethyl)-N-[2-[3-[(2-hydroxyethyl)thio]-2,5-dioxo-1-pyrrolidinyl]ethyl]glycyl-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide, (1'→1''')-amide with 12-oxo-2,5,8,11-tetraoxa-13-azahexadecan-16-oic acid [1-[(2S,4S)-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-4-[[2,3,6-trideoxy-3-[[[[4-[(L-phenylalanyl-L-lysyl)amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-2-naphthacenyl]-2-hydroxyethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



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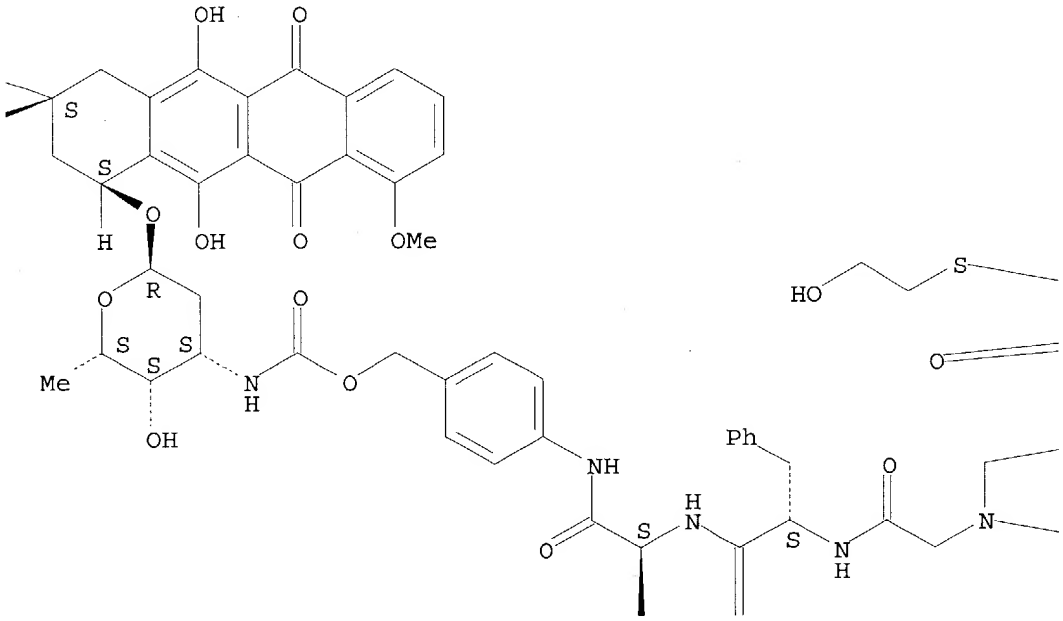
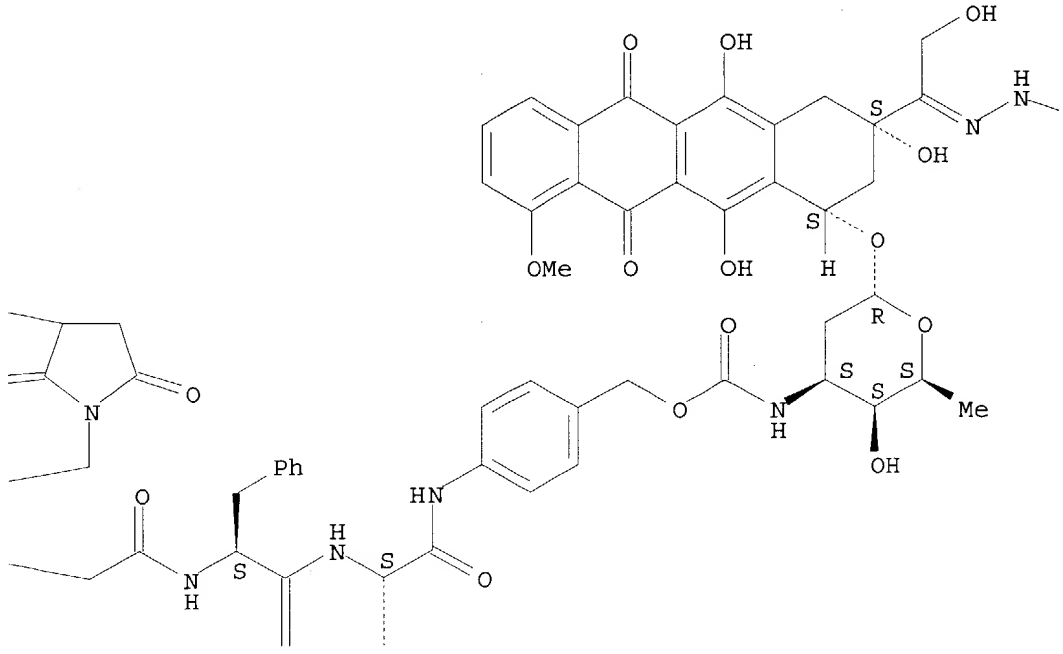
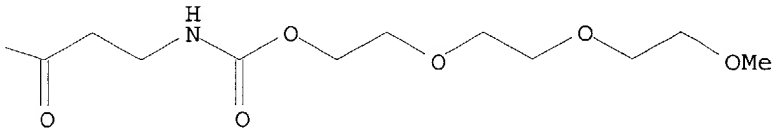


PAGE 1-C

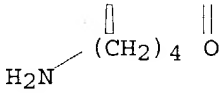


Searched by P. Ruppel

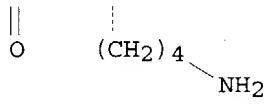
PAGE 1-D



PAGE 2-B



PAGE 2-C



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:453441 HCAPLUS
DOCUMENT NUMBER: 137:190578
TITLE: Cathepsin B-Labile Dipeptide Linkers for Lysosomal Release of Doxorubicin from Internalizing Immunoconjugates: Model Studies of Enzymatic Drug Release and Antigen-Specific In Vitro Anticancer Activity
AUTHOR(S): Dubowchik, Gene M.; Firestone, Raymond A.; Padilla, Linda; Willner, David; Hofstead, Sandra J.; Mosure, Kathleen; Knipe, Jay O.; Lasch, Shirley J.; Trail, Pamela A.
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT, 06492, USA
SOURCE: Bioconjugate Chemistry (2002), 13(4), 855-869
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The anticancer drug doxorubicin (DOX) was linked to chimeric BR96, an internalizing monoclonal antibody that binds to a Lewisy-related, tumor-associated antigen, through 2 lysosomally cleavable dipeptides, Phe-Lys and Val-Cit, giving immunoconjugates (I and II). A self-immolative p-aminobenzyloxycarbonyl (PABC) spacer between the dipeptides and the DOX was required for rapid and quant. generation of free drug. DOX release from the model substrate Z-Phe-Lys-PABC-DOX was 30-fold faster than from Z-Val-Cit-PABC-DOX with the cysteine protease cathepsin B alone, but rates were identical in a rat liver lysosomal preparation suggesting the

participation of more than one enzyme. Conjugates I and II showed rapid and near quant. drug release with cathepsin B and in a lysosomal preparation, while demonstrating excellent stability in human plasma. Against tumor cell lines with varying levels of BR96 expression, both conjugates showed potent, antigen-specific cytotoxic activity, suggesting that they will be effective in delivering DOX selectively to antigen-expressing carcinomas.

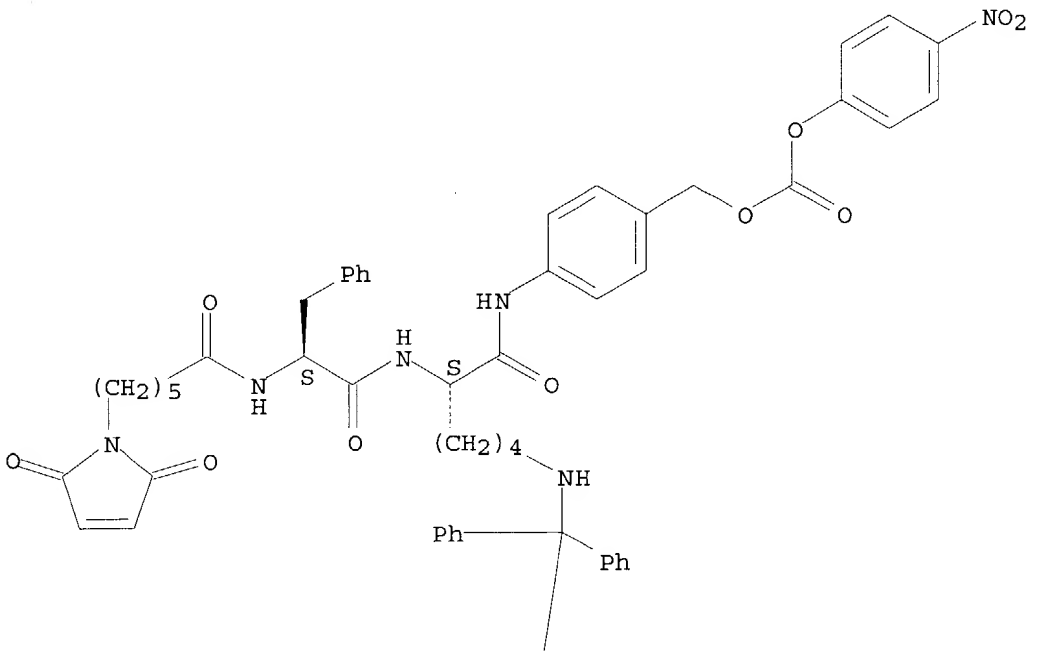
IT **159857-66-6P 159857-67-7P 159857-69-9P**
159857-70-2P 159857-81-5P 159857-90-6P
159857-91-7P 159857-95-1P 159857-96-2P
159858-08-9P 220369-57-3P 448963-35-7P
448963-36-8P 448963-37-9P 448963-38-0P
448963-39-1P 448963-40-4P 448963-41-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cathepsin B-labile peptide linkers for lysosomal release of doxorubicin from internalizing immunoconjugates in relation to anticancer activity)

RN 159857-66-6 HCAPLUS

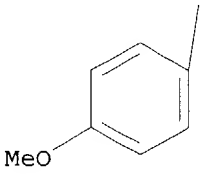
CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



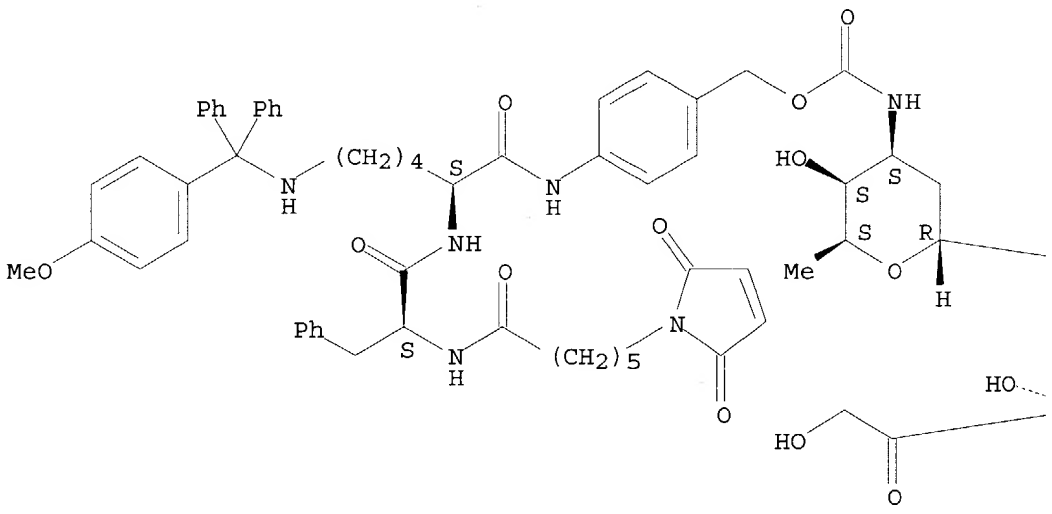
PAGE 2-A



RN 159857-67-7 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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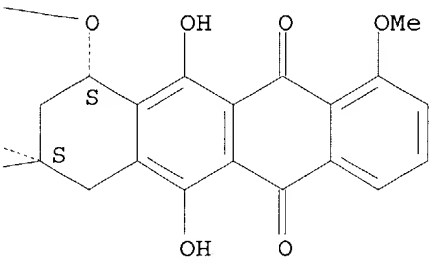


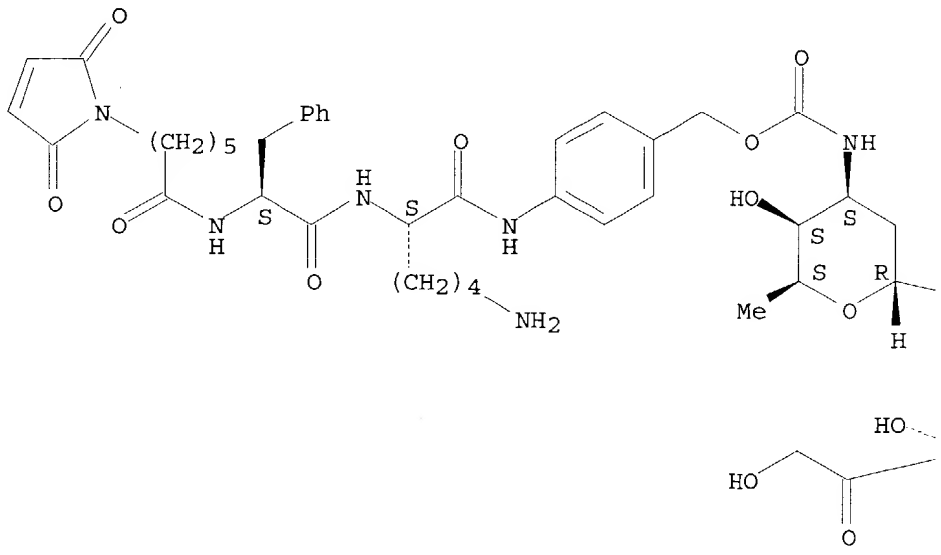
RN 159857-69-9 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,,10S)-, mono(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 159857-68-8
CMF C60 H68 N6 O18

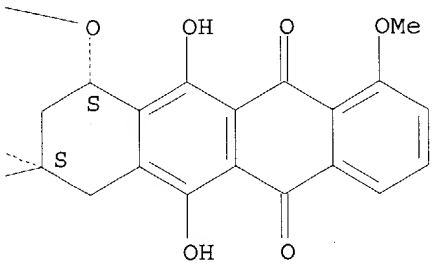
Absolute stereochemistry.

PAGE 1-A



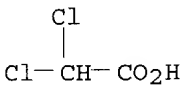
Searched by P. Ruppel

PAGE 1-B



CM 2

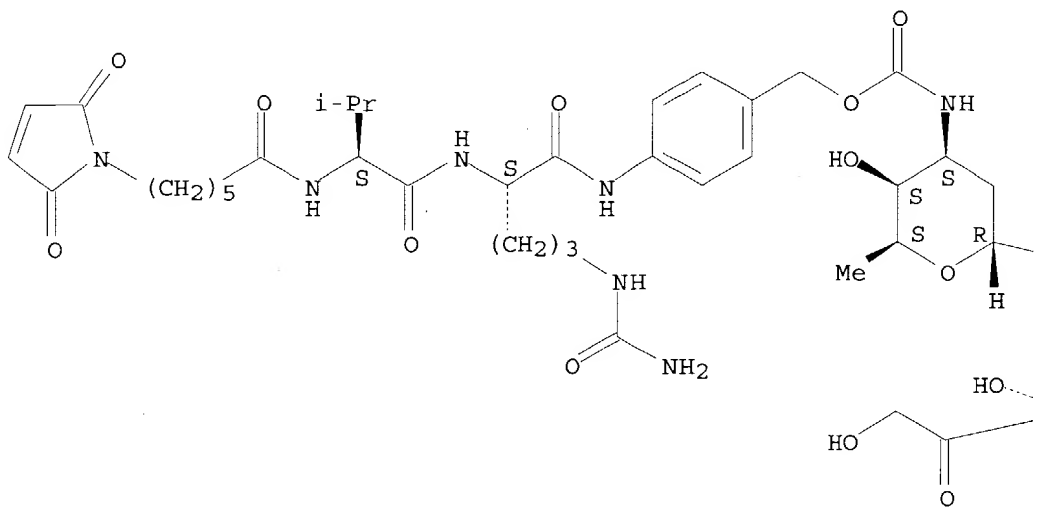
CRN 79-43-6
CMF C2 H2 Cl2 O2



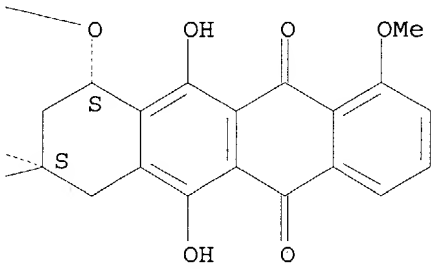
RN 159857-70-2 HCAPLUS
CN 5,12-Naphthacenedione, 10-[[3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-valyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

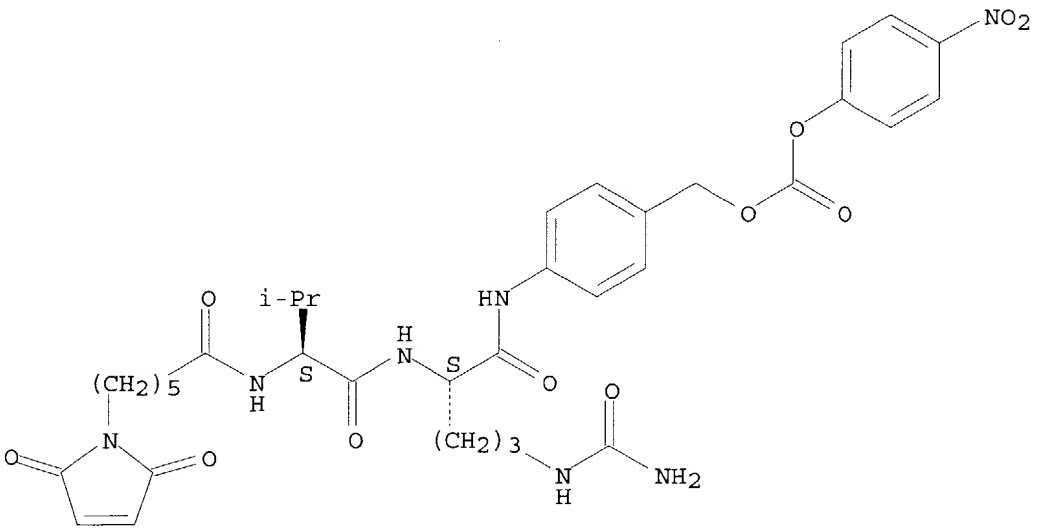


PAGE 1-B



RN 159857-81-5 HCAPLUS
CN L-Ornithinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-valyl-N5-(aminocarbonyl)-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

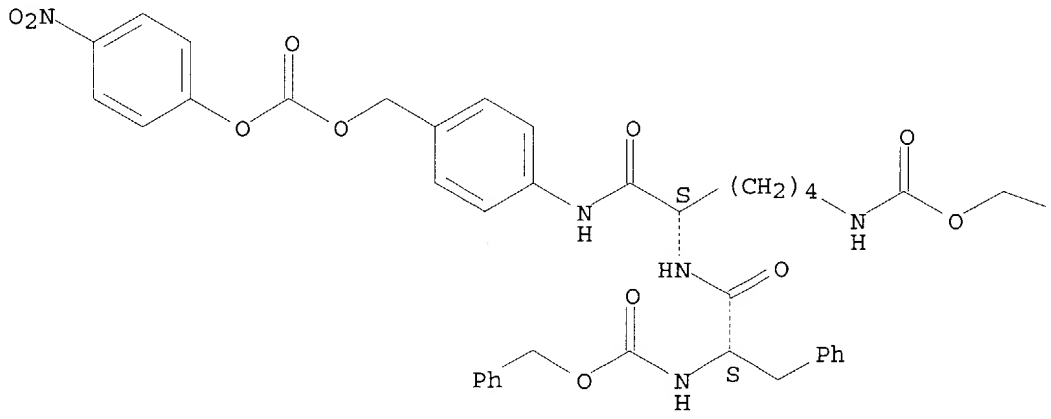
Absolute stereochemistry.



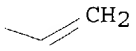
RN 159857-90-6 HCAPLUS
CN L-Lysinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-N6-[(2-propenyloxy)carbonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



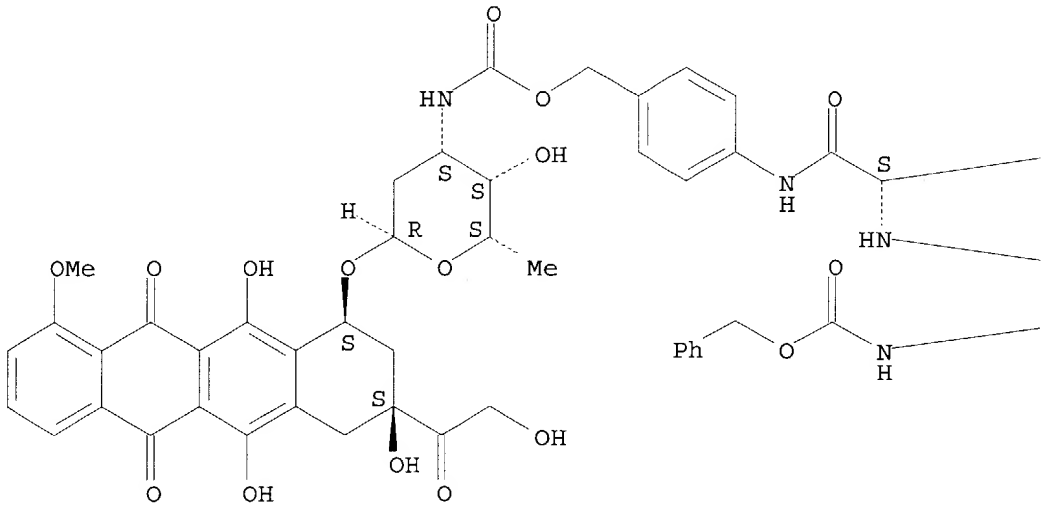
PAGE 1-B



RN 159857-91-7 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N6-[(2-propenyloxy)carbonyl]-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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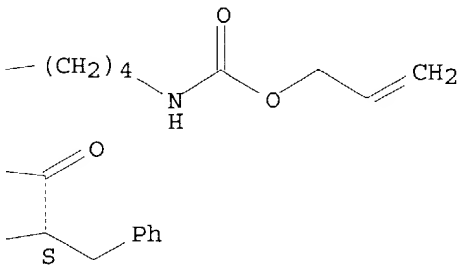
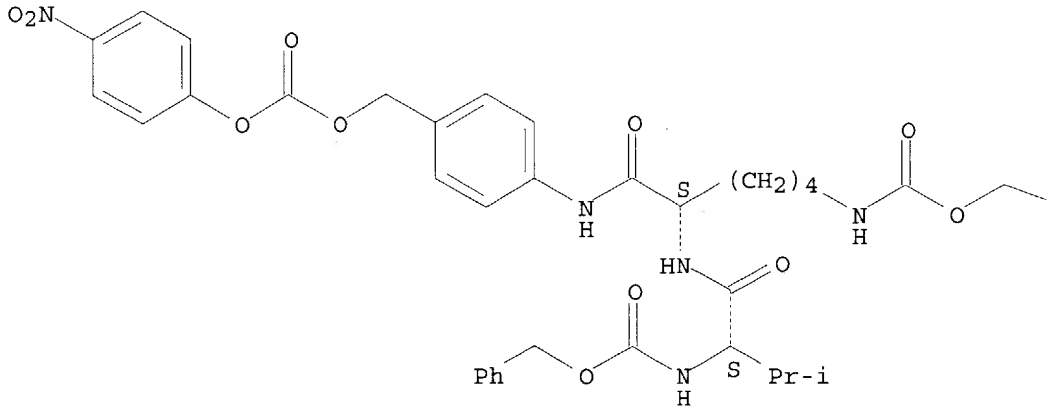


RN 159857-95-1 HCAPLUS
CN L-Lysinamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-N6-[(2-propenyloxy)carbonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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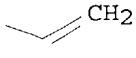
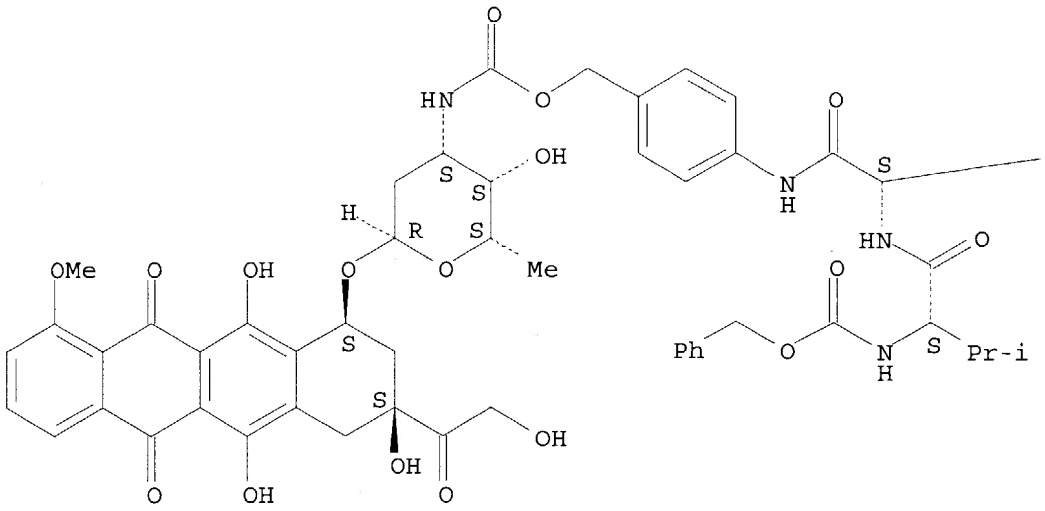


RN 159857-96-2 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-

[(phenylmethoxy)carbonyl]-L-valyl-N6-[(2-propenyloxy)carbonyl]-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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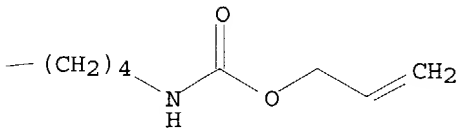
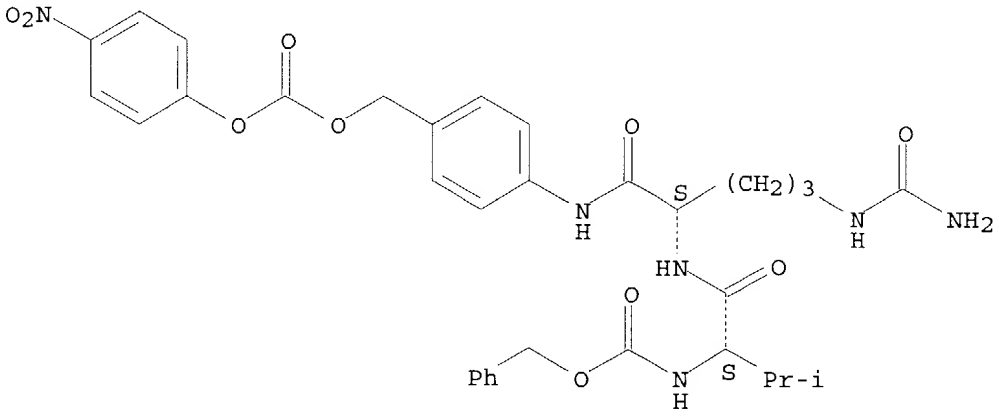


RN 159858-08-9 HCAPLUS
CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N5-(aminocarbonyl)-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

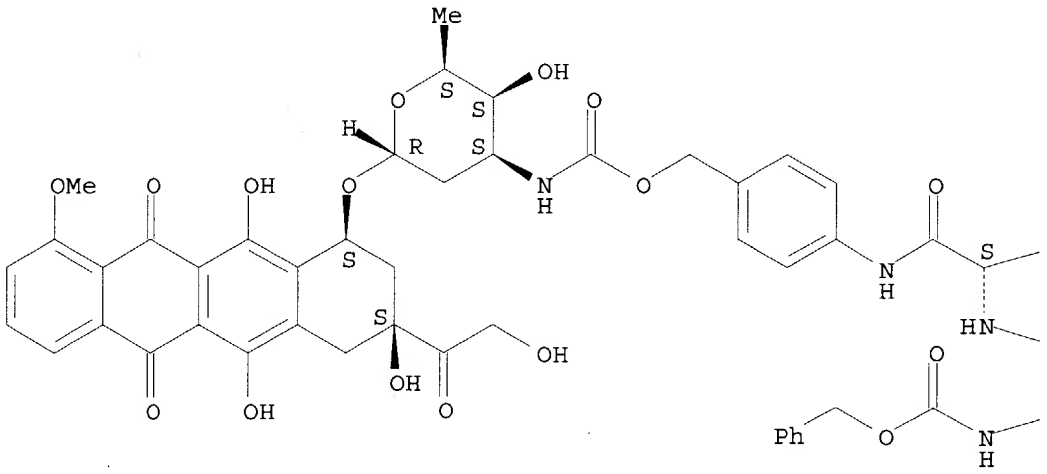
Absolute stereochemistry.



RN 220369-57-3 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-alanyl-N6-[(2-propenyloxy)carbonyl]-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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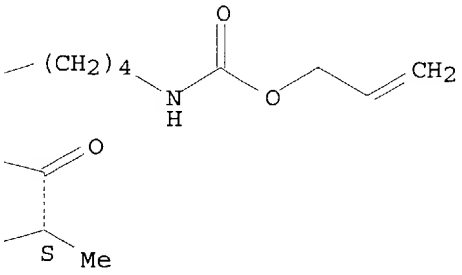
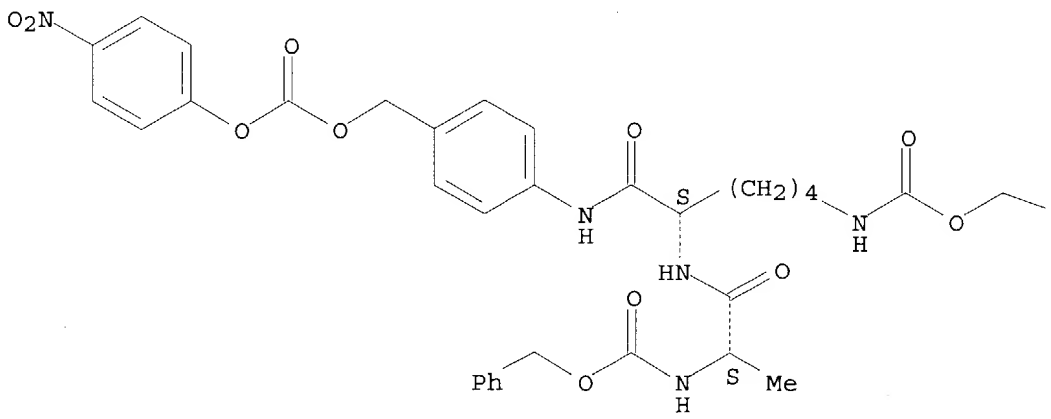


RN 448963-35-7 HCAPLUS
CN L-Lysinamide, N-[(phenylmethoxy)carbonyl]-L-alanyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-N6-[(2-propenyloxy)carbonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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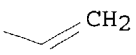
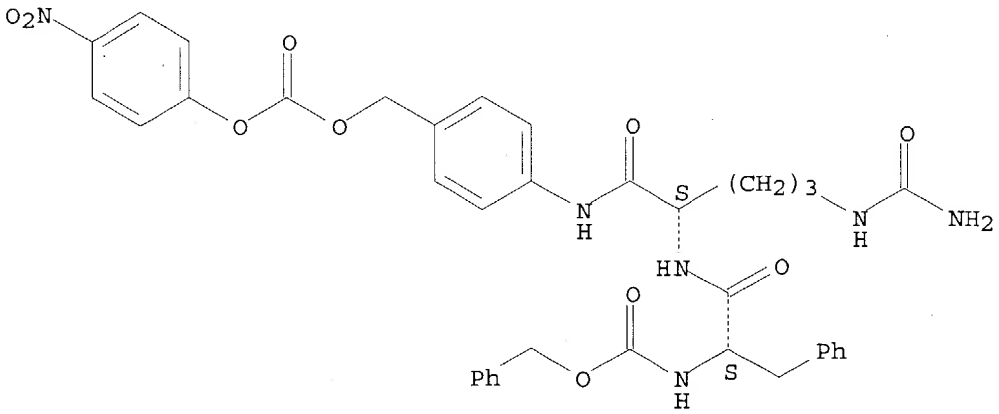


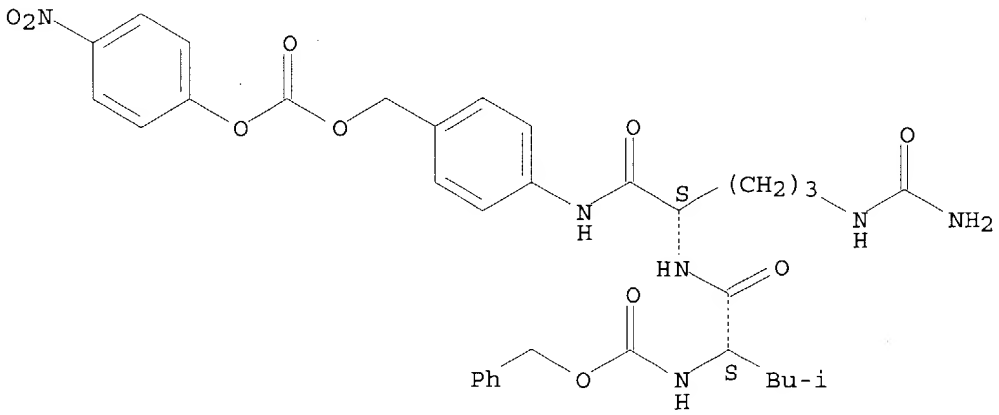
RN 448963-36-8 HCAPLUS
CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N5-(aminocarbonyl)-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



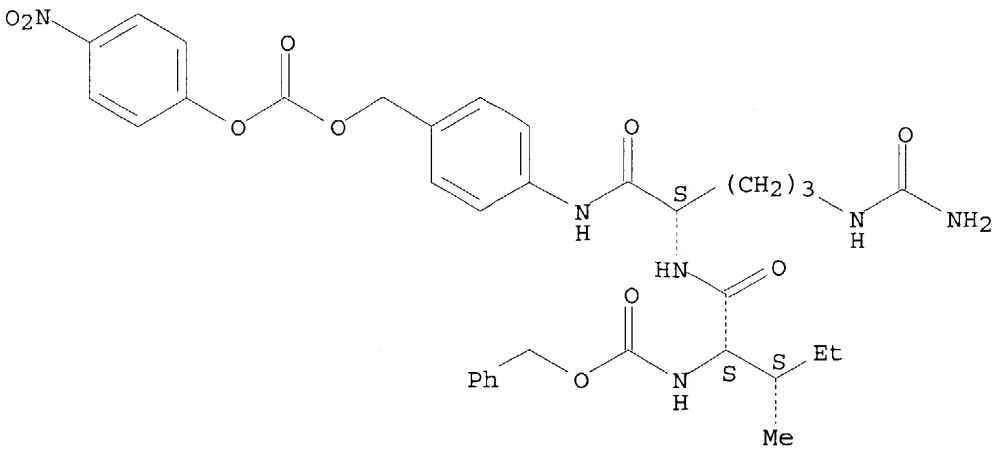
RN 448963-37-9 HCAPLUS
CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N5-(aminocarbonyl)-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



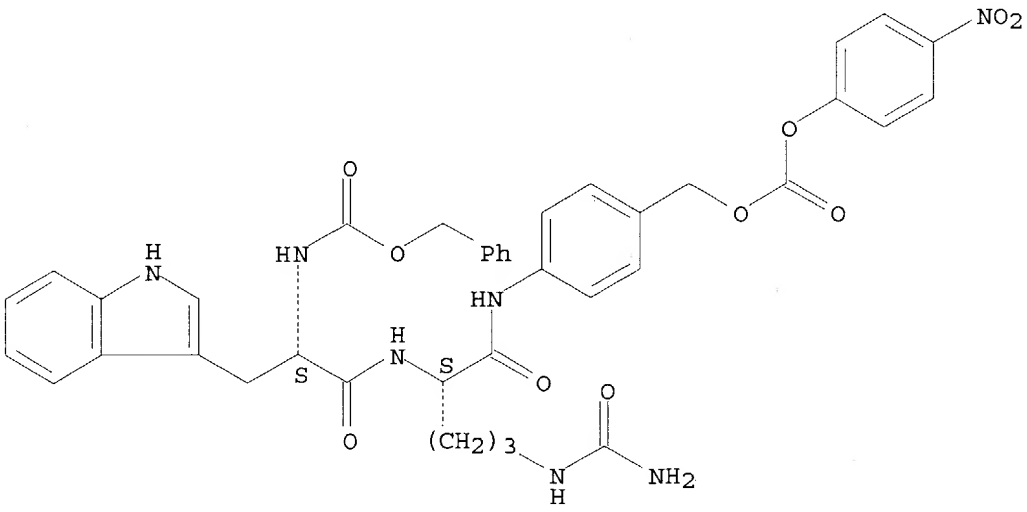
RN 448963-38-0 HCAPLUS
CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-isoleucyl-N5-(aminocarbonyl)-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



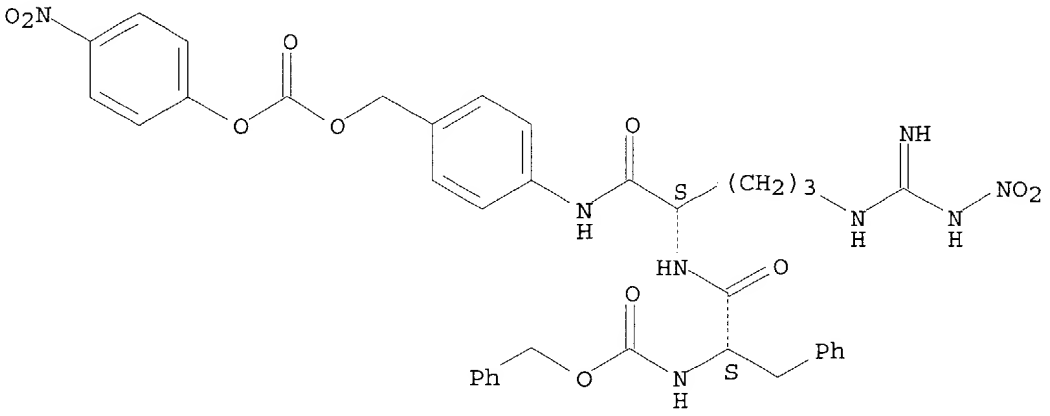
RN 448963-39-1 HCAPLUS
CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-tryptophyl-N5-(aminocarbonyl)-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 448963-40-4 HCAPLUS
CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N5-[imino(nitroamino)methyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

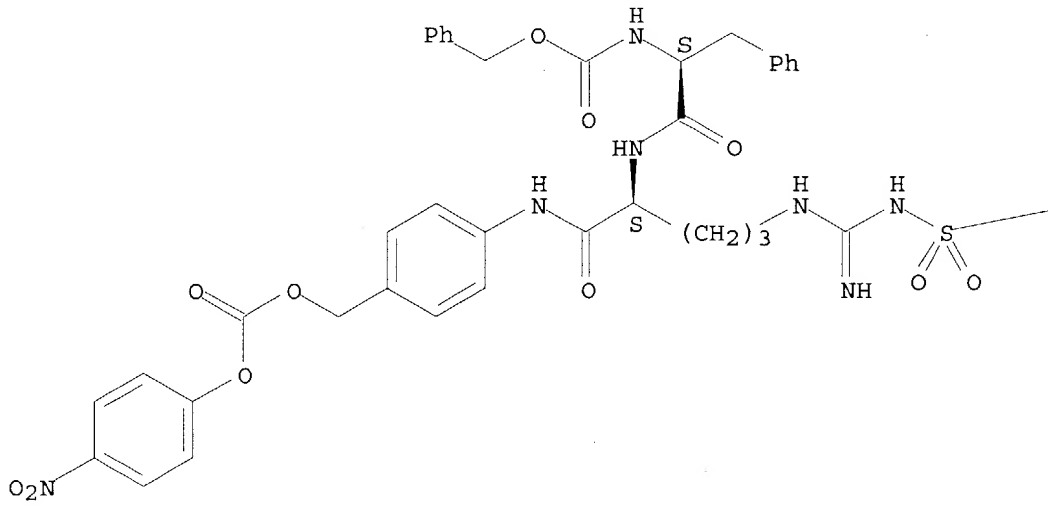
Absolute stereochemistry.



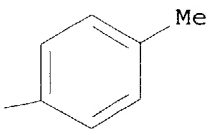
RN 448963-41-5 HCAPLUS
CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT **159857-69-9DP, conjugates** with antibodies
159857-70-2DP, conjugates with antibodies
159857-92-8P 159857-97-3P 159858-09-0P
220369-64-2P 220369-65-3P 220369-66-4P
220369-67-5P 220369-68-6P 220369-69-7P
448963-42-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cathepsin B-labile peptide linkers for lysosomal release of doxorubicin from internalizing immunoconjugates in relation to anticancer activity)

RN 159857-69-9 HCAPLUS

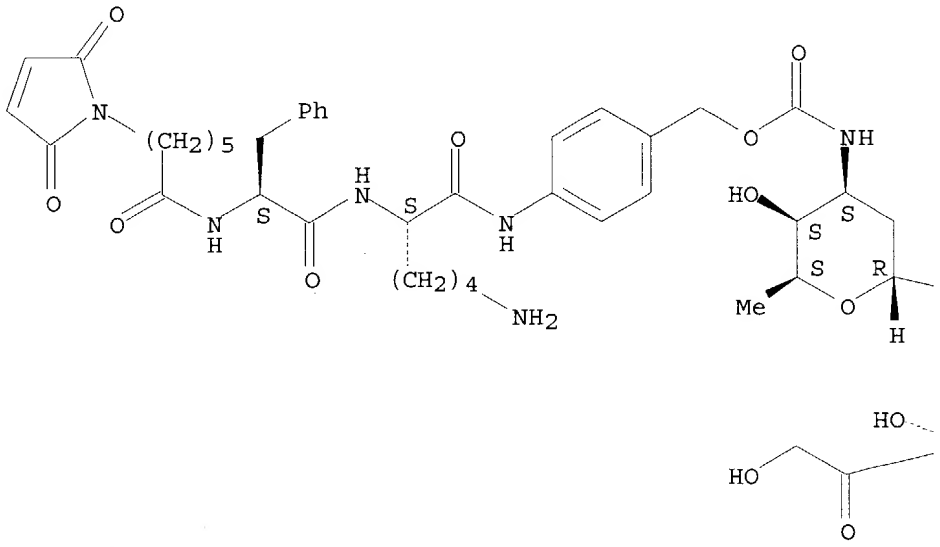
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,,10S)-, mono(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

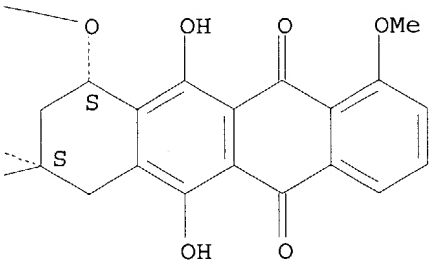
CRN 159857-68-8
CMF C60 H68 N6 O18

Absolute stereochemistry.

PAGE 1-A

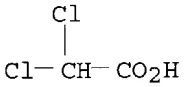


PAGE 1-B



CM 2

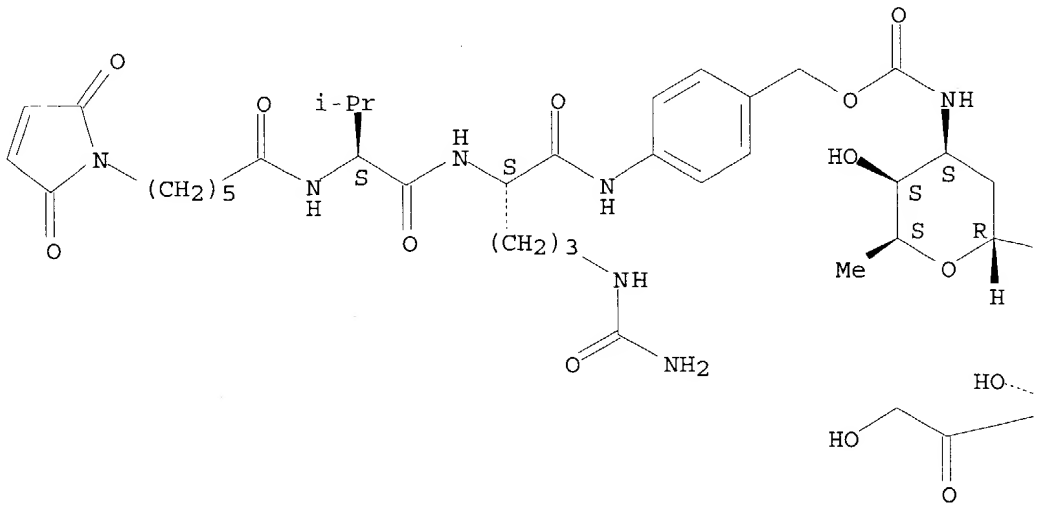
CRN 79-43-6
CMF C2 H2 Cl2 O2



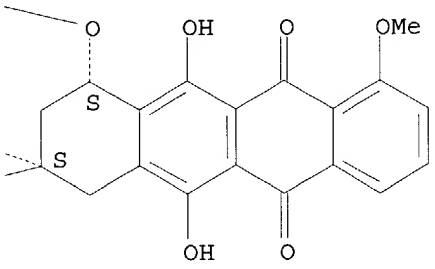
RN 159857-70-2 HCAPLUS
CN 5,12-Naphthacenedione, 10-[[3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-valyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



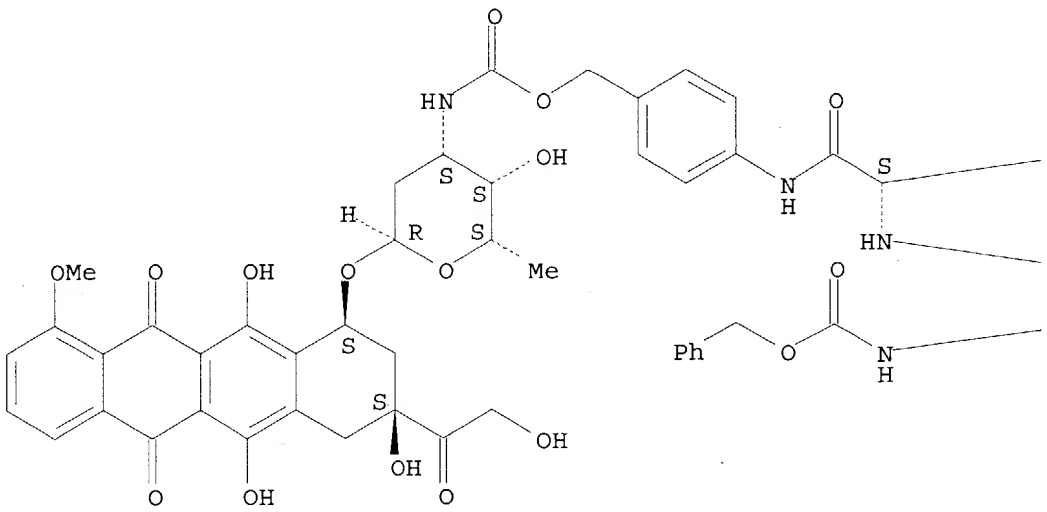
PAGE 1-B



RN 159857-92-8 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, monohydrochloride, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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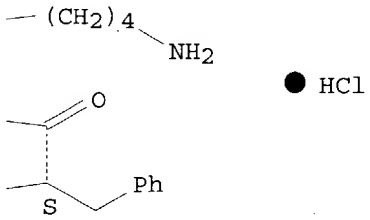
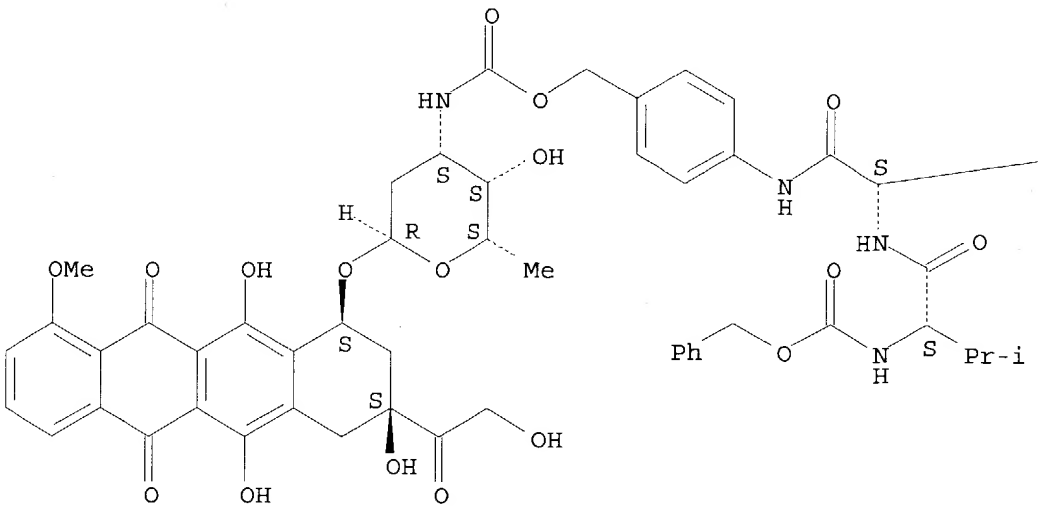


RN 159857-97-3 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-valyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, monohydrochloride, (8S,10S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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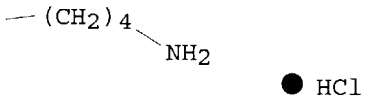
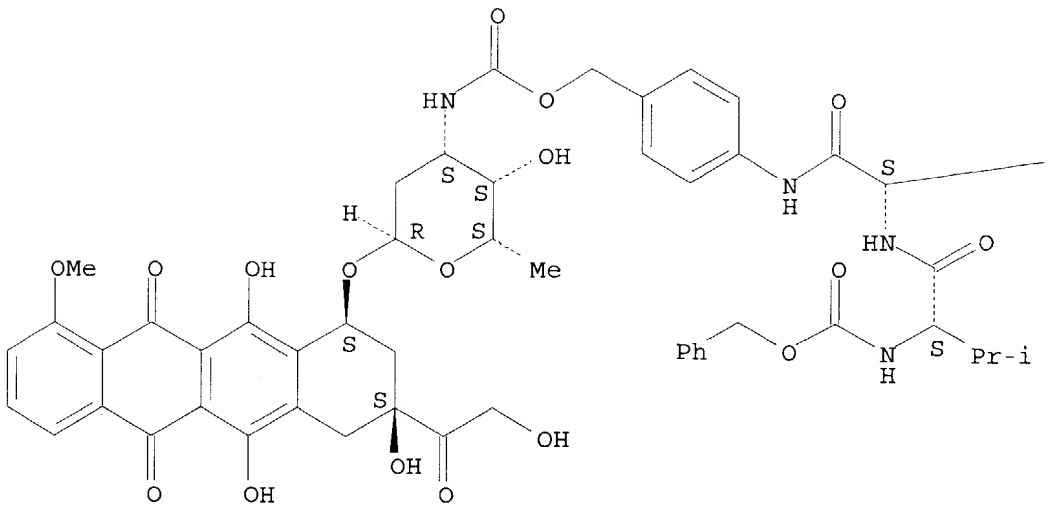


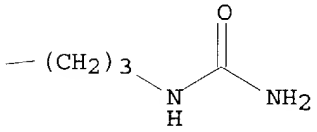
RN 159858-09-0 HCAPLUS
CN 5,12-Naphthacenedione, 10-[[3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-valyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



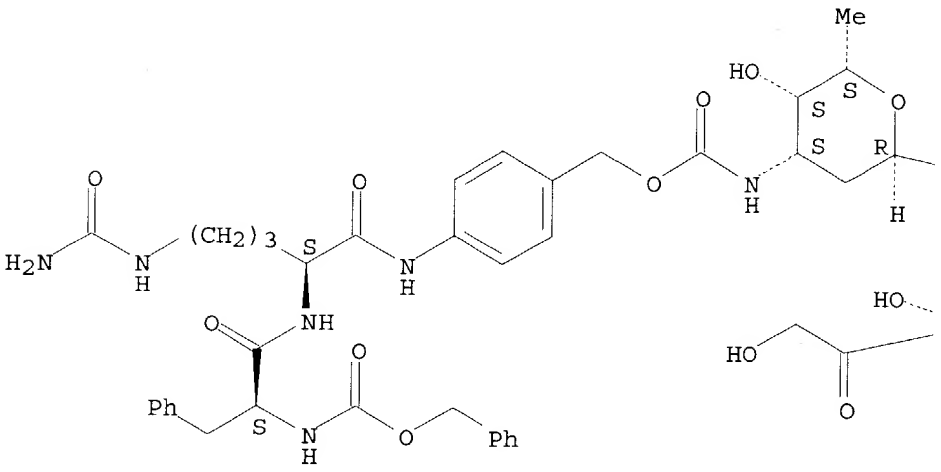
PAGE 1-B



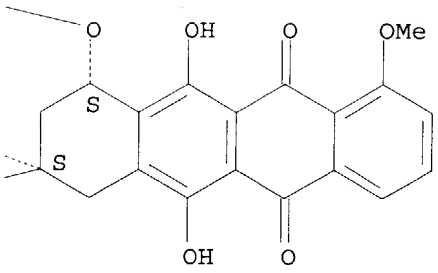
RN 220369-64-2 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



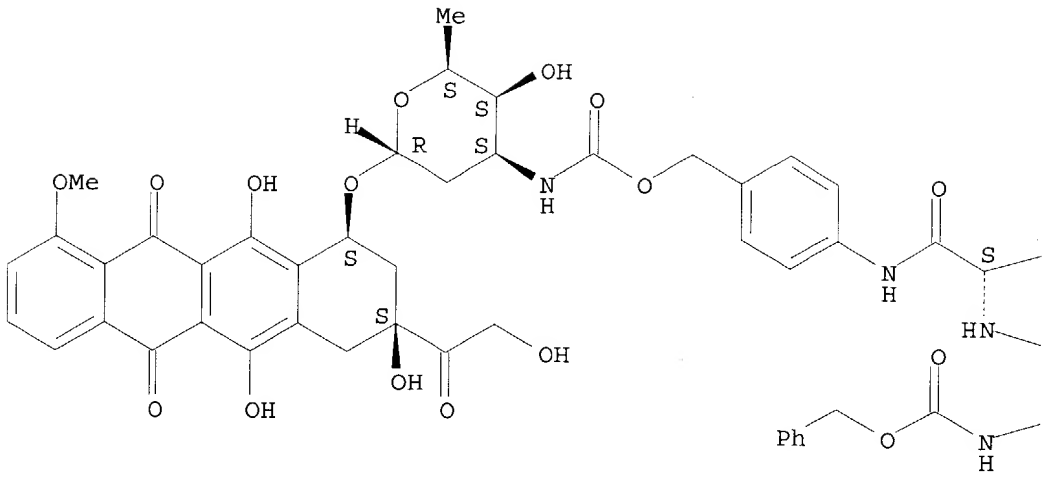
PAGE 1-B



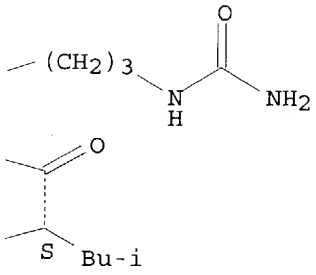
RN 220369-65-3 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-leucyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



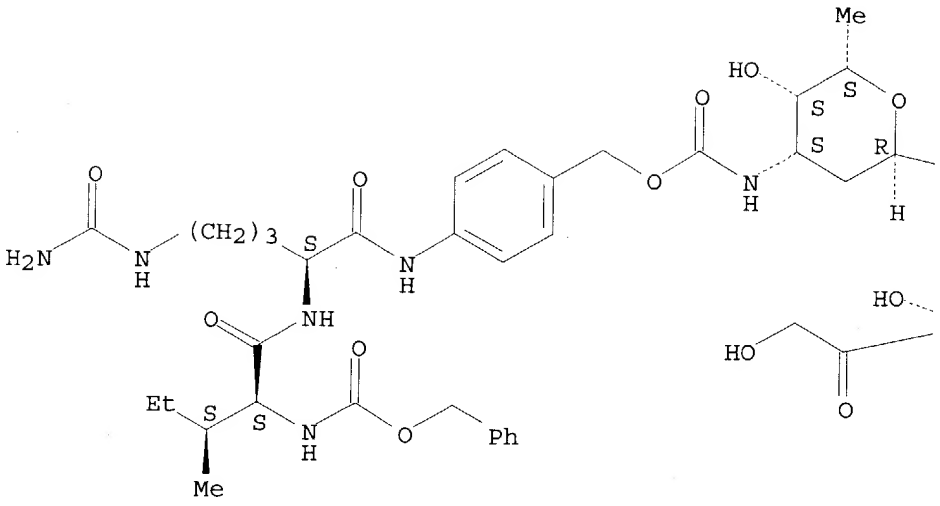
PAGE 1-B



RN 220369-66-4 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-isoleucyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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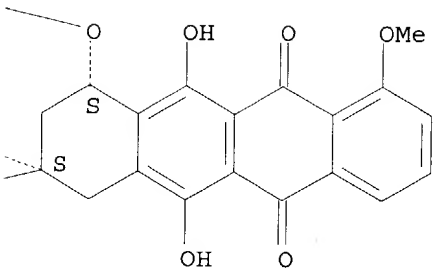
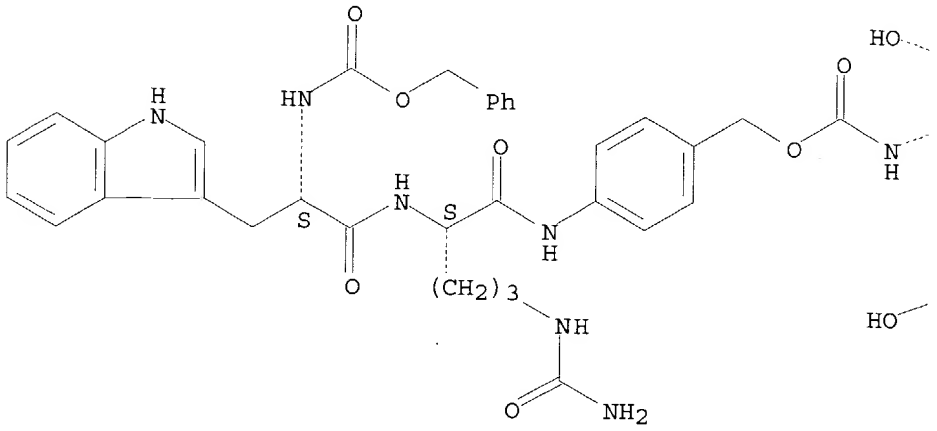


RN 220369-67-5 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-tryptophyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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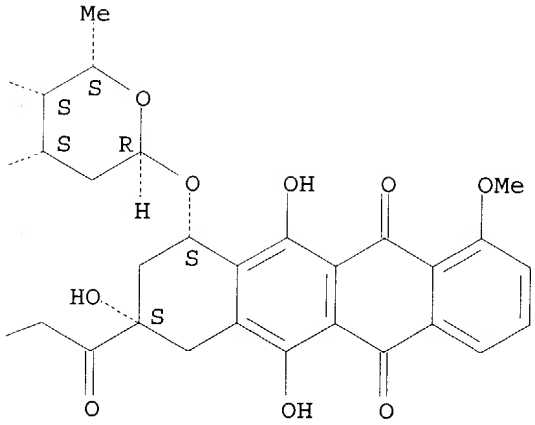
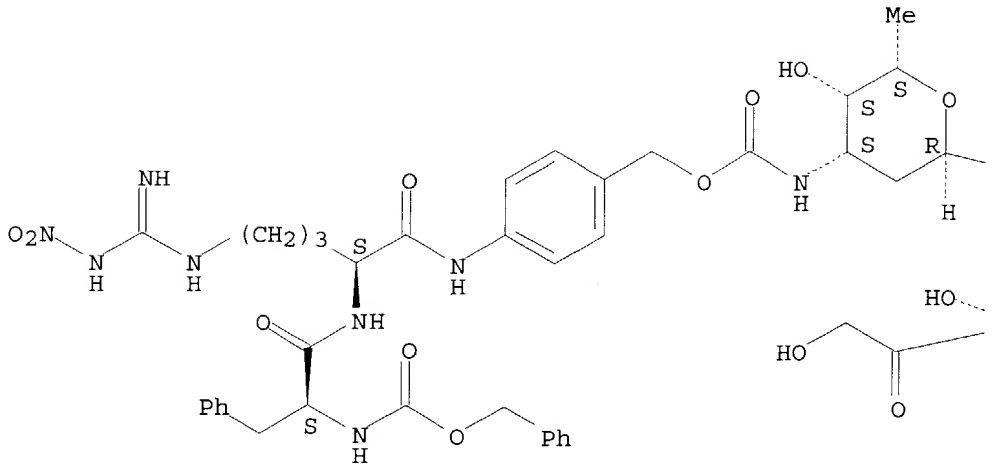


RN 220369-68-6 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N5-[imino(nitroamino)methyl]-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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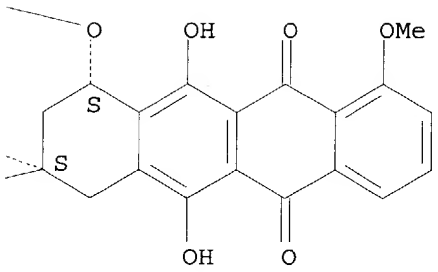
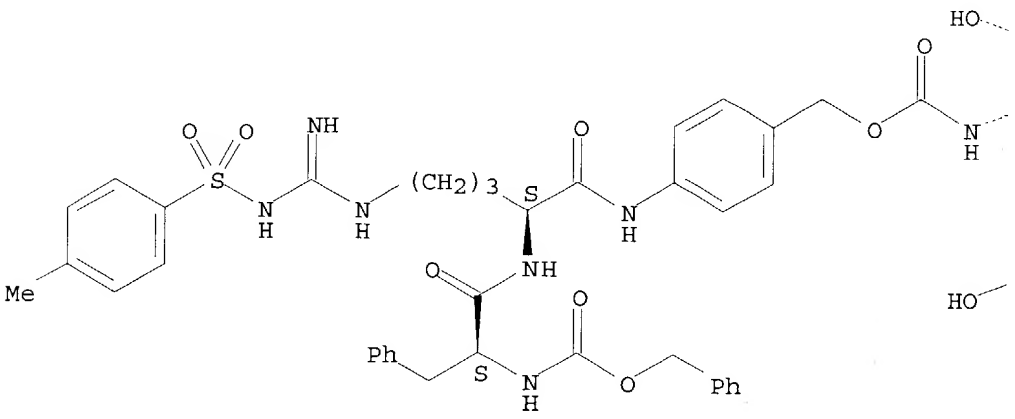


RN 220369-69-7 HCAPLUS

CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N5-[imino[[(4-methylphenyl)sulfonyl]amino]methyl]-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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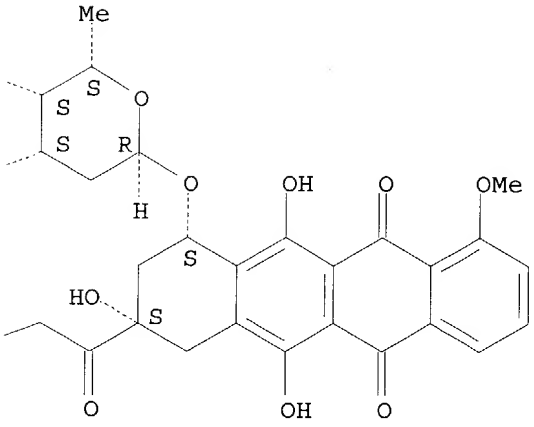
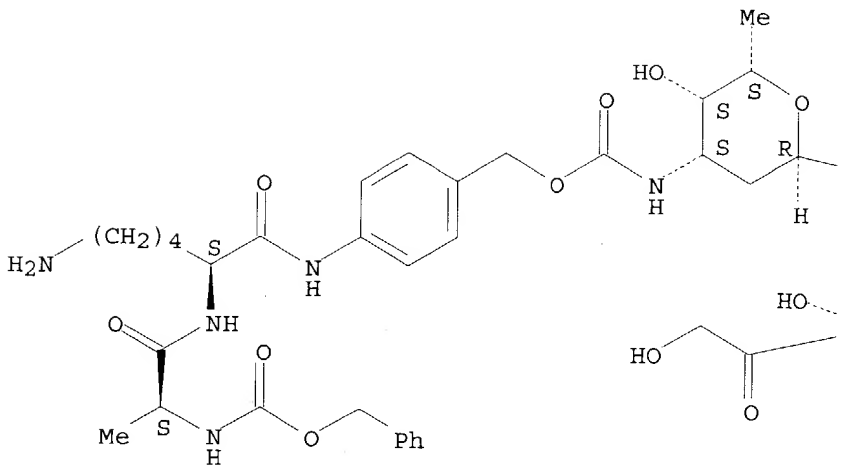


RN 448963-42-6 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-alanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, monohydrochloride, (8S,10S)-(9CI) (CA INDEX NAME)

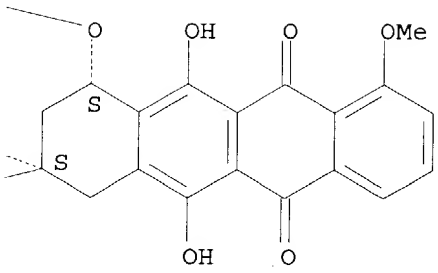
Absolute stereochemistry.

PAGE 1-A



● HCl

PAGE 1-B



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:379641 HCAPLUS
DOCUMENT NUMBER: 138:210058
TITLE: Doxorubicin immunoconjugates containing bivalent, lysosomally-cleavable dipeptide linkages
AUTHOR(S): Dubowchik, Gene M.; Radia, Shilpa; Mastalerz, Harold; Walker, Michael A.; Firestone, Raymond A.; King, H. Dalton; Hofstead, Sandra J.; Willner, David; Lasch, Shirley J.; Trail, Pamela A.
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research

Searched by P. Ruppel

Institute, Wallingford, CT, 06492-7660, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(11), 1529-1532
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Bivalent doxorubicin (DOX)-dipeptides were prepared and conjugated to the monoclonal antibody BR96. The dipeptides are cleaved by lysosomal proteases following internalization of the resulting immunoconjugates. Conjugate I (R = BR96) demonstrated antigen-specific in vitro tumor cell killing activity (IC50=0.2 μM) that was equipotent to DOX with a near doubling of drug mols./MAb. Size exclusion chromatog. showed I to be a noncovalent dimer that was formed immediately upon conjugation.

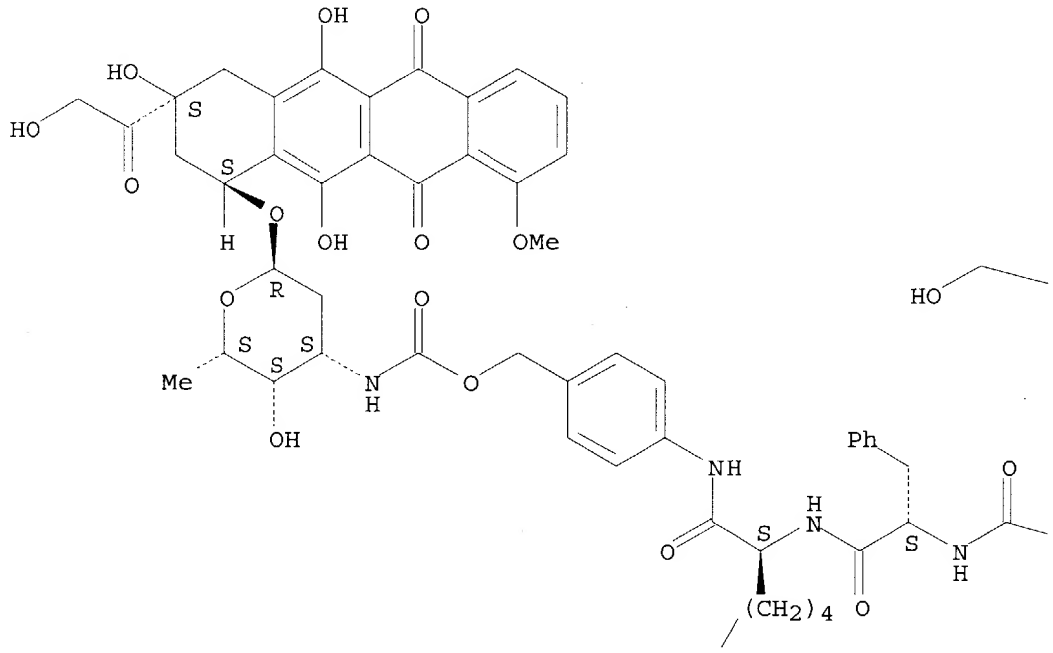
IT **499137-64-3P**
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor activity of doxorubicin **conjugate** with monoclonal antibody BR96)

RN 499137-64-3 HCAPLUS

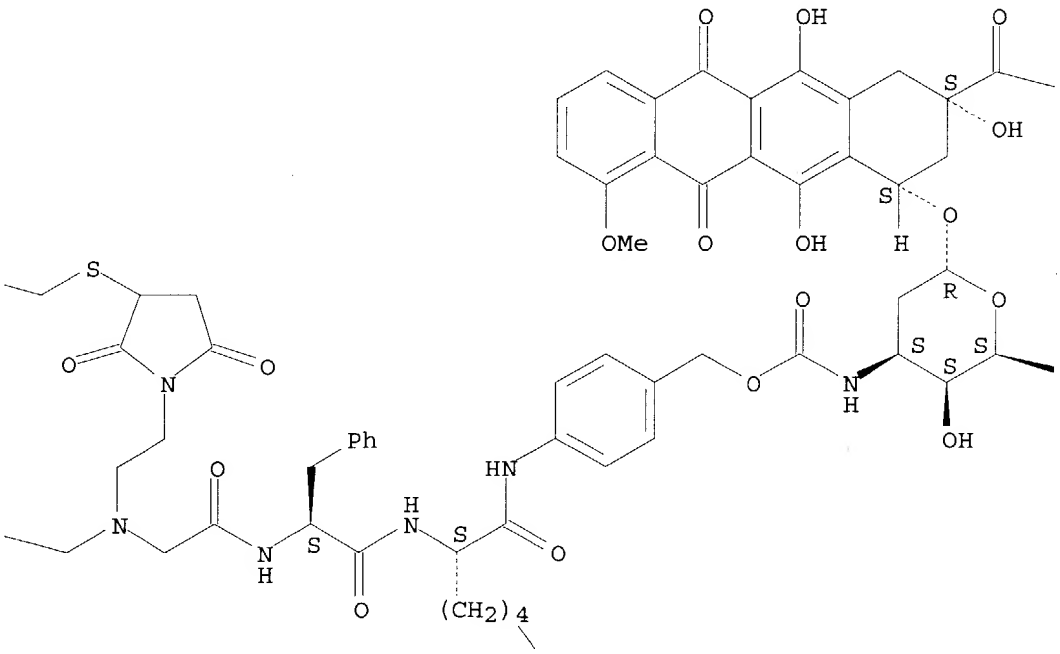
CN L-Lysinamide, 1,1'-[[[2-[3-[(2-hydroxyethyl)thio]-2,5-dioxo-1-pyrrolidinyl]ethyl]imino]bis(1-oxo-2,1-ethanediyl)]bis[L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



Searched by P. Ruppel

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PAGE 2-A

PAGE 2-B

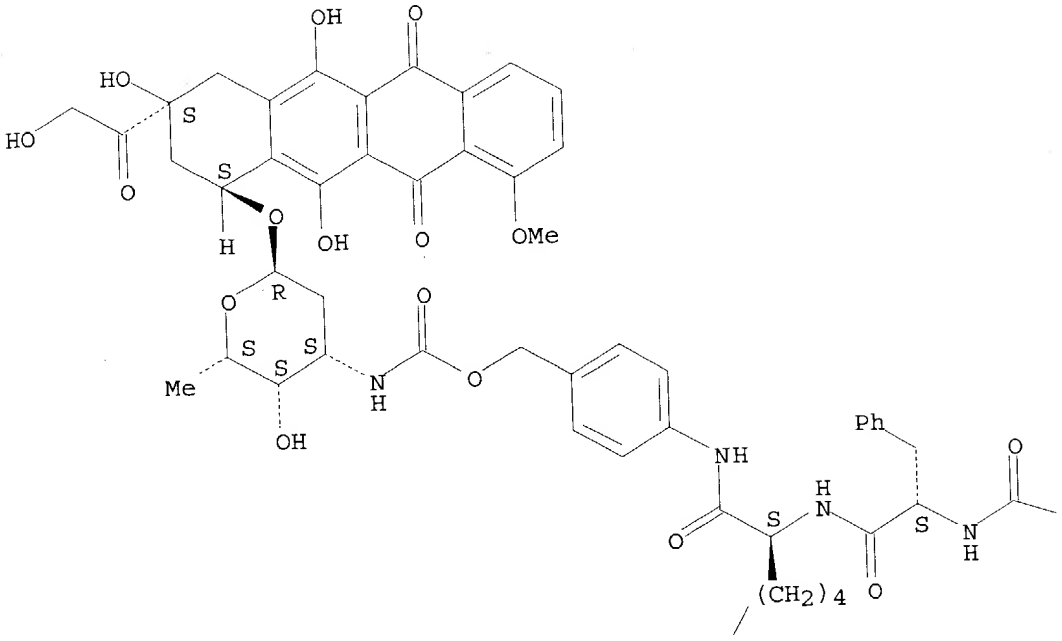
IT **499137-65-4DP, conjugate** with monoclonal antibody BR96
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of doxorubicin **conjugate** with monoclonal antibody BR96)

RN 499137-65-4 HCAPLUS

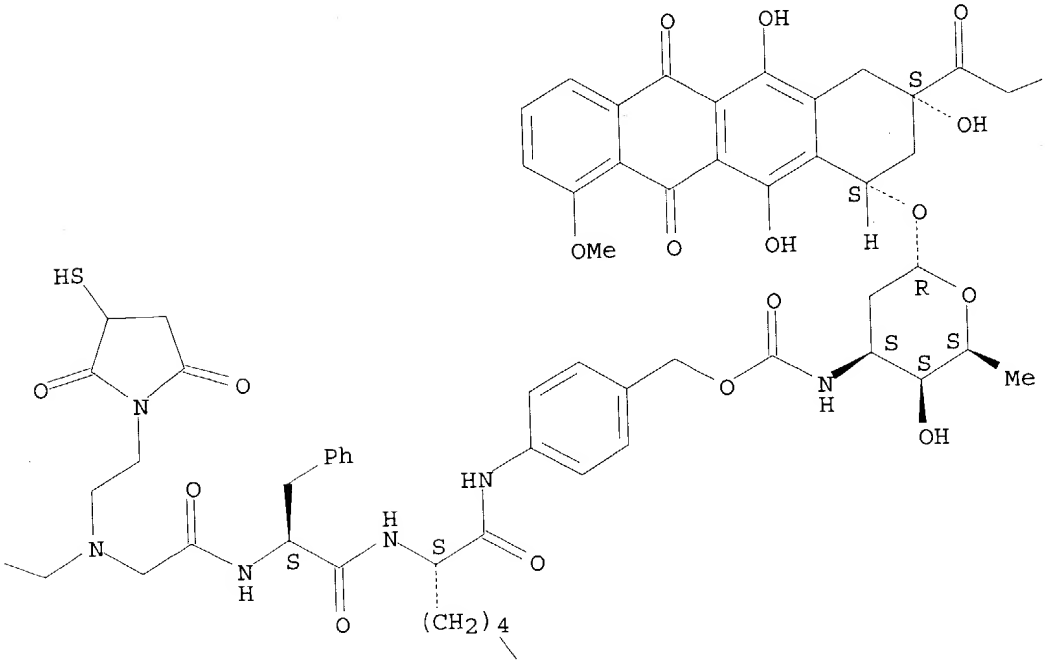
CN L-Lysinamide, 1,1'-[[[2-(3-mercapto-2,5-dioxo-1-pyrrolidinyl)ethyl]imino]bis(1-oxo-2,1-ethanediyl)]bis[L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



Searched by P. Ruppel

PAGE 1-C

PAGE 2-A

PAGE 2-B

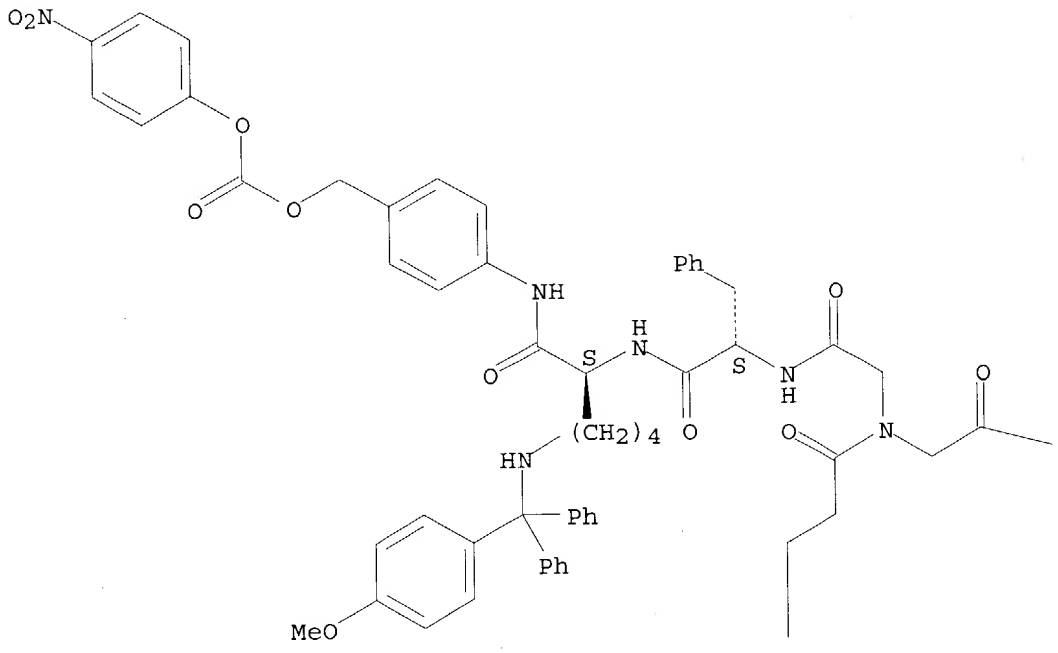
IT **207613-16-9P 207613-17-0P 207613-65-8P**
207613-68-1P 207613-79-4P 207613-81-8P
207613-83-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor activity of doxorubicin **conjugate** with monoclonal antibody BR96)

RN 207613-16-9 HCAPLUS

CN L-Lysinamide, N-(carboxymethyl)-N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]glycyl-L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-, (1→1')-amide with L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-L-lysinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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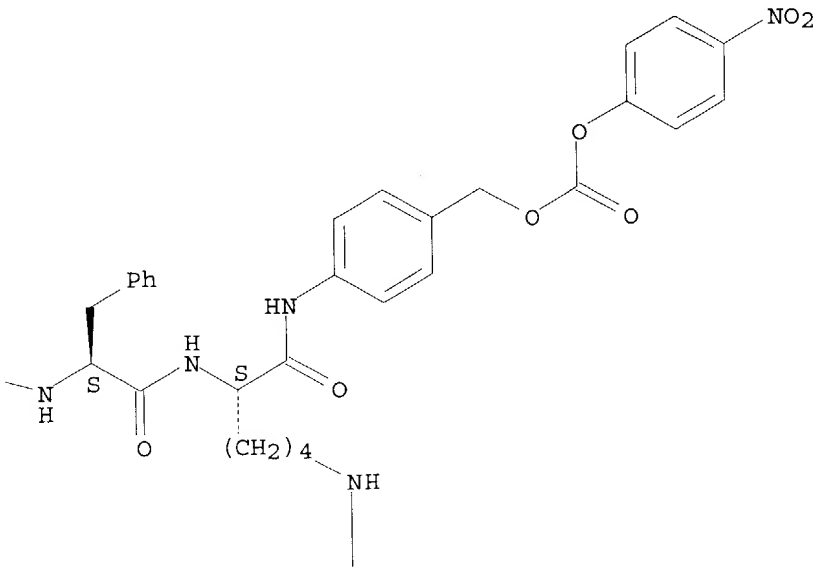
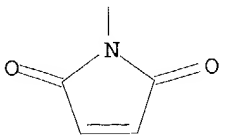


Searched by P. Ruppel

PAGE 2-A



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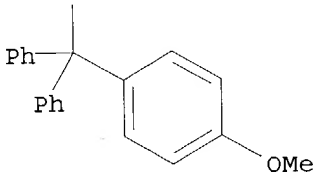
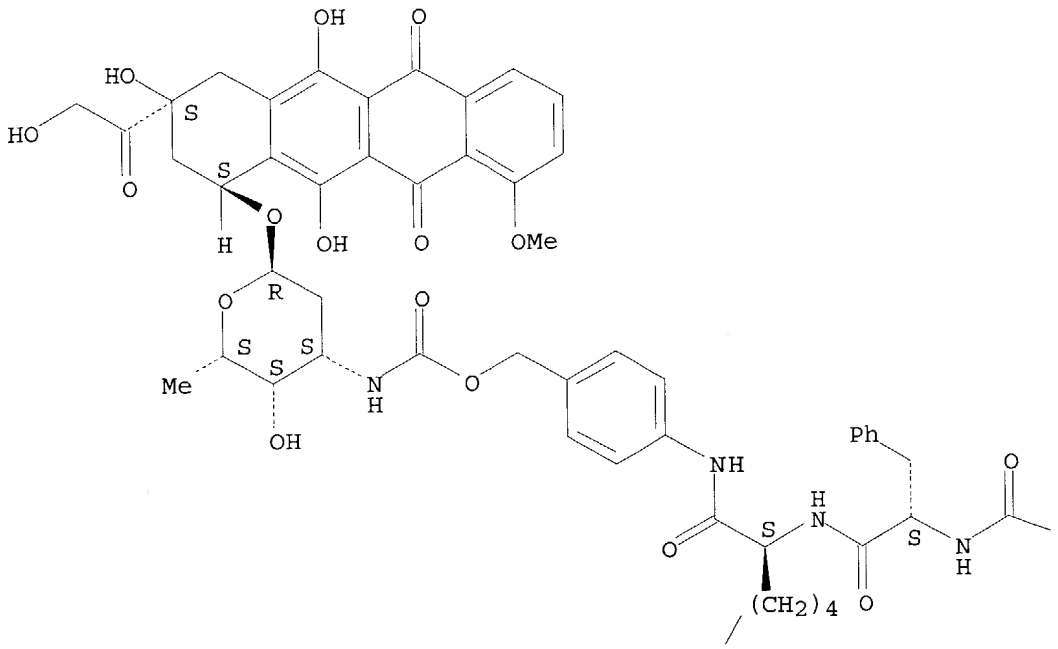


RN 207613-17-0 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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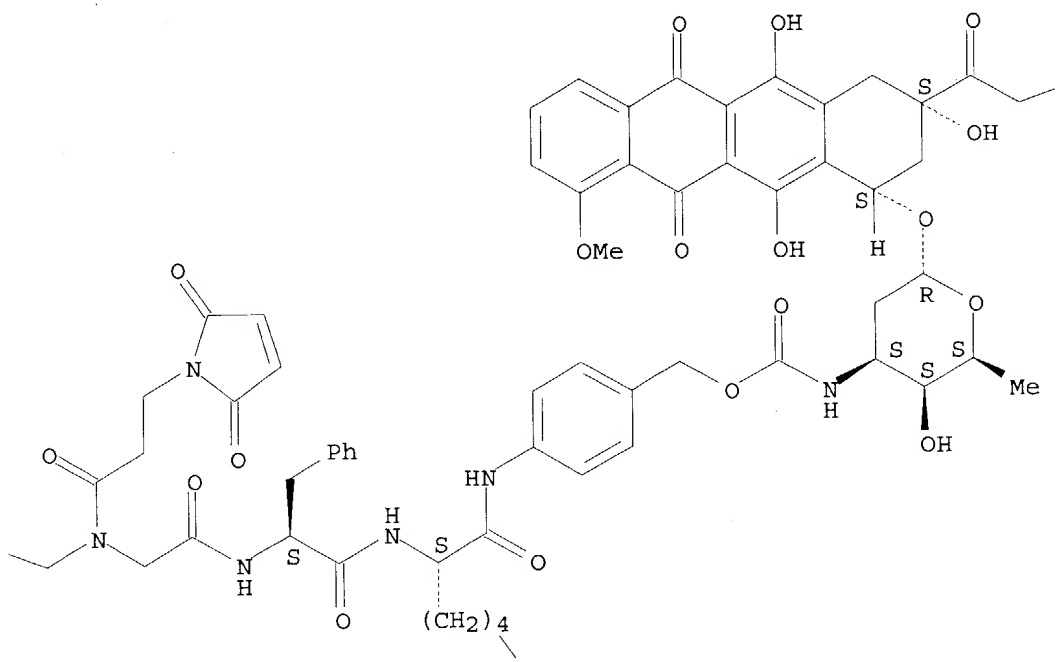
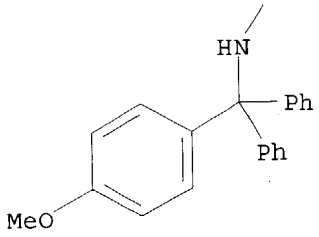


Searched by P. Ruppel

PAGE 1-C

PAGE 2-A



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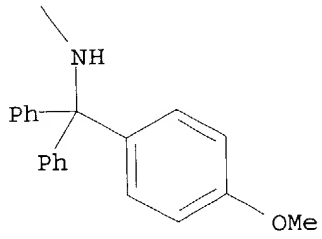

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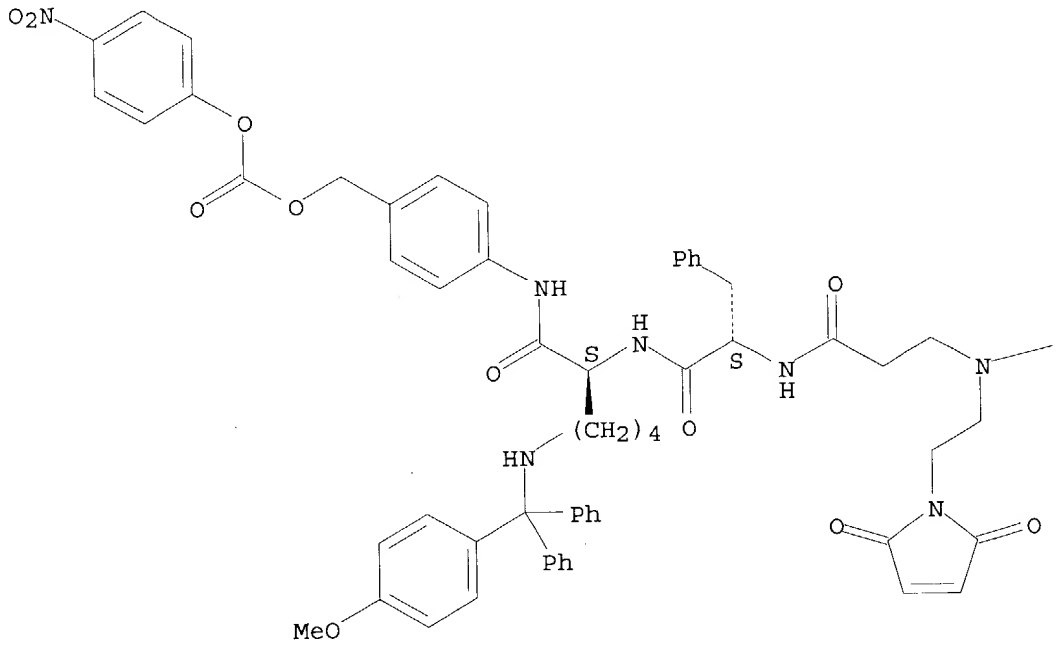
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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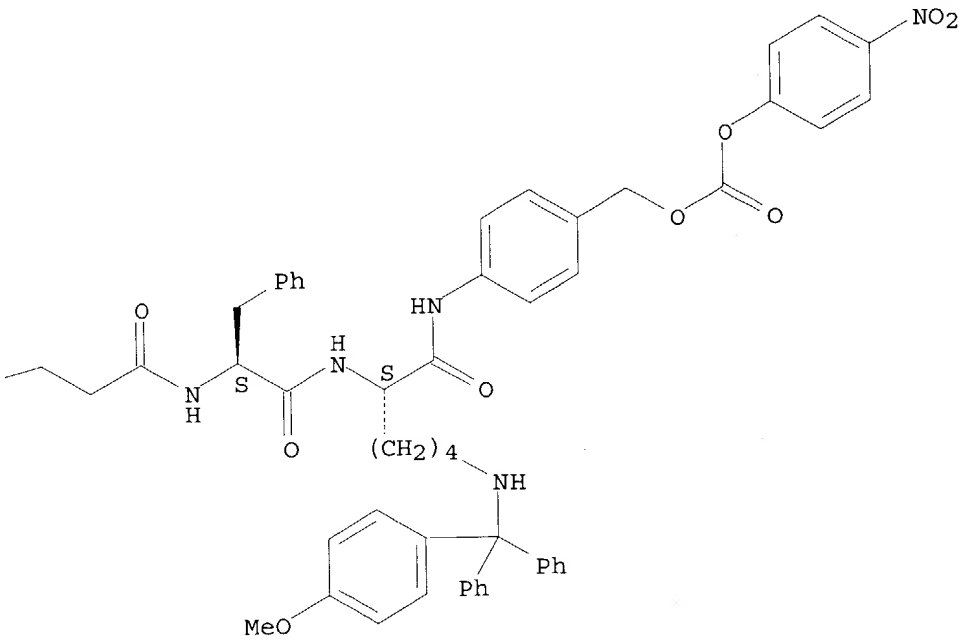
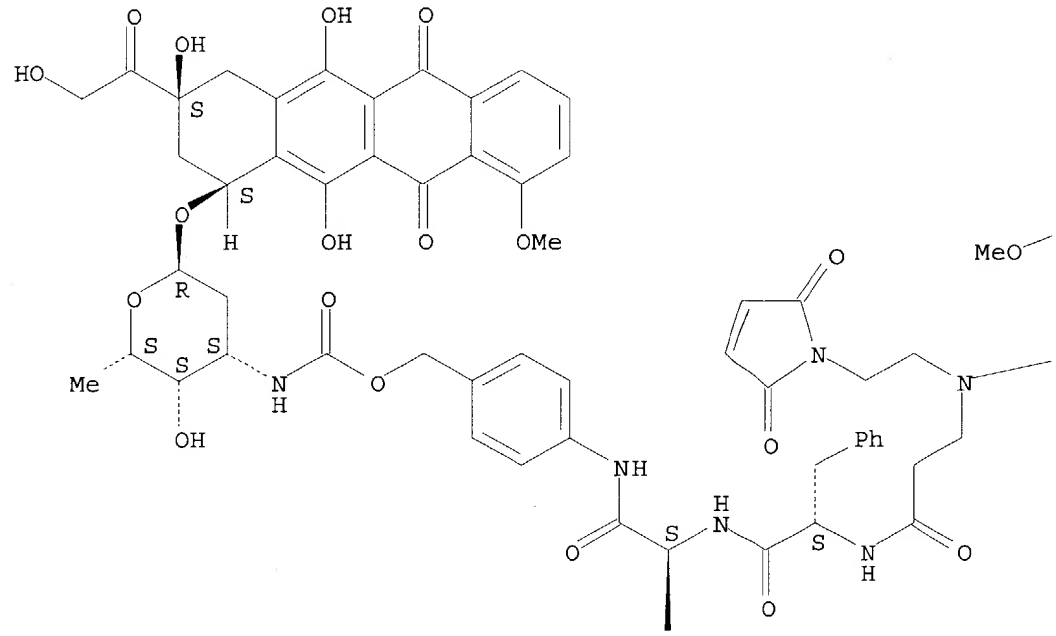


RN 207613-68-1 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, diester with

(8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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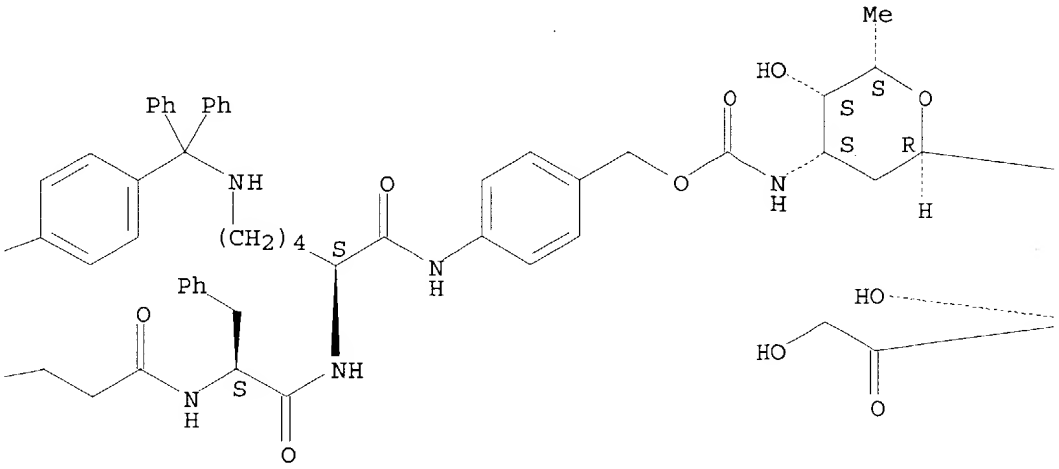

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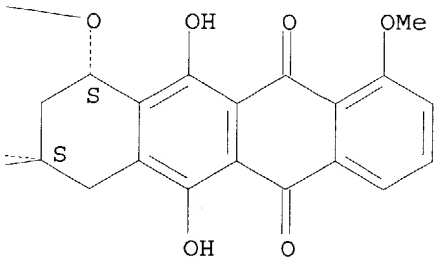

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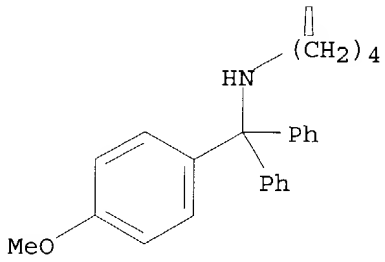
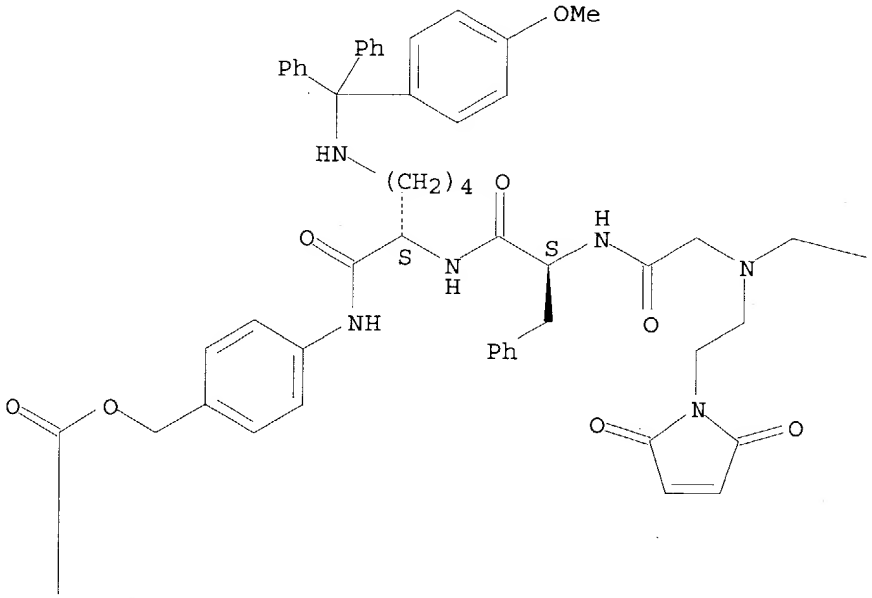


RN 207613-79-4 HCAPLUS

CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-, (1→1')-amide with L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-L-lysinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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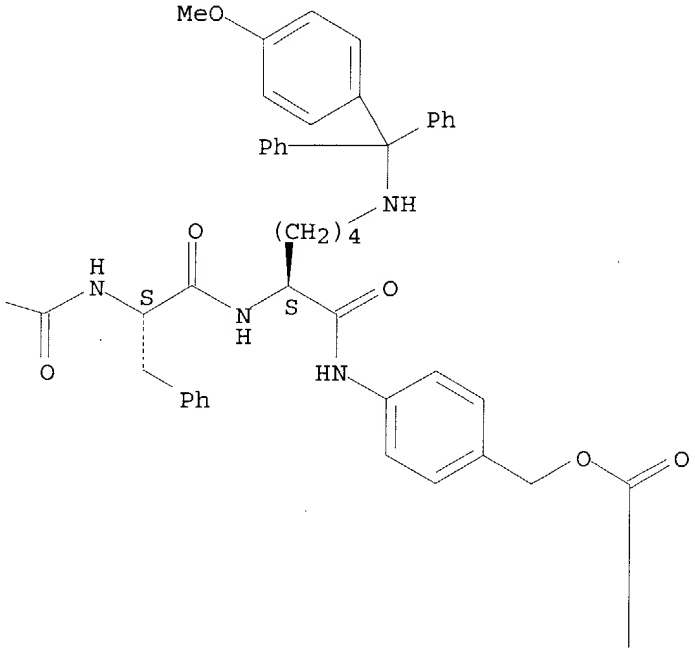
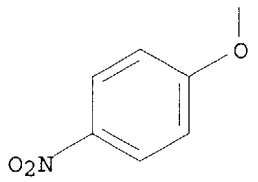


Searched by P. Ruppel

PAGE 2-A



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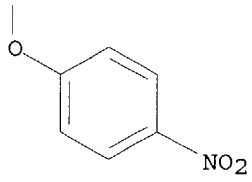
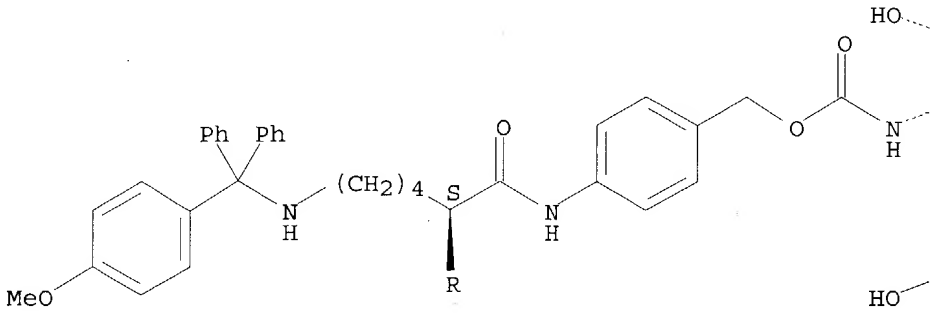
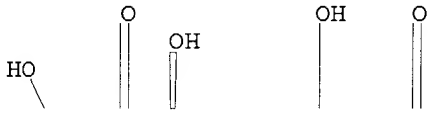


RN 207613-81-8 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





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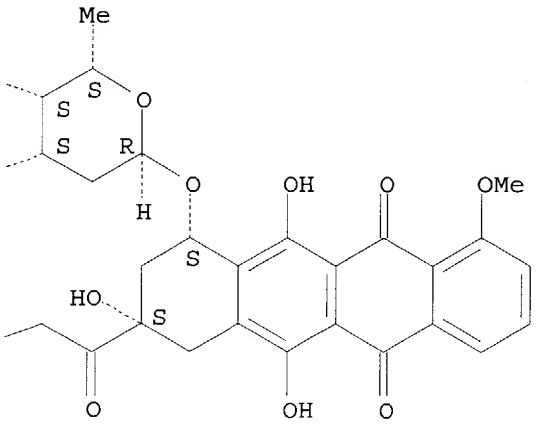

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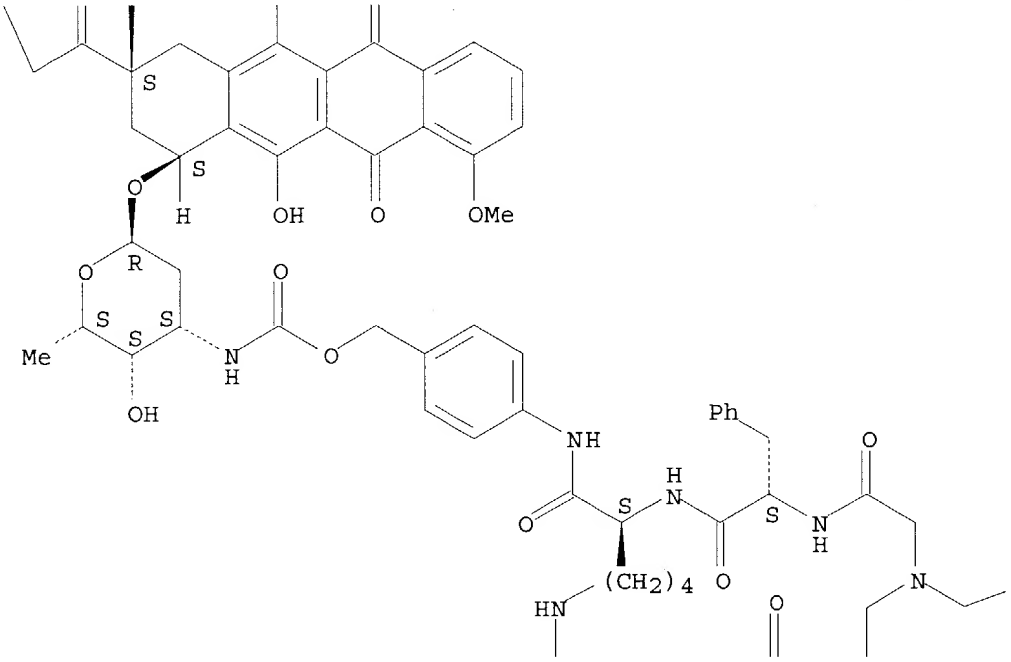

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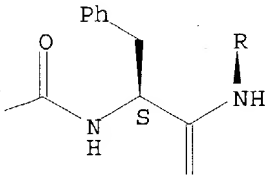

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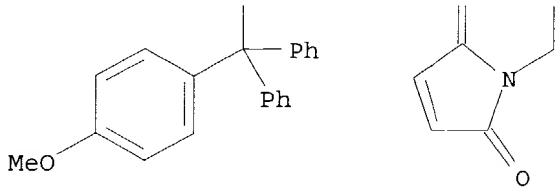


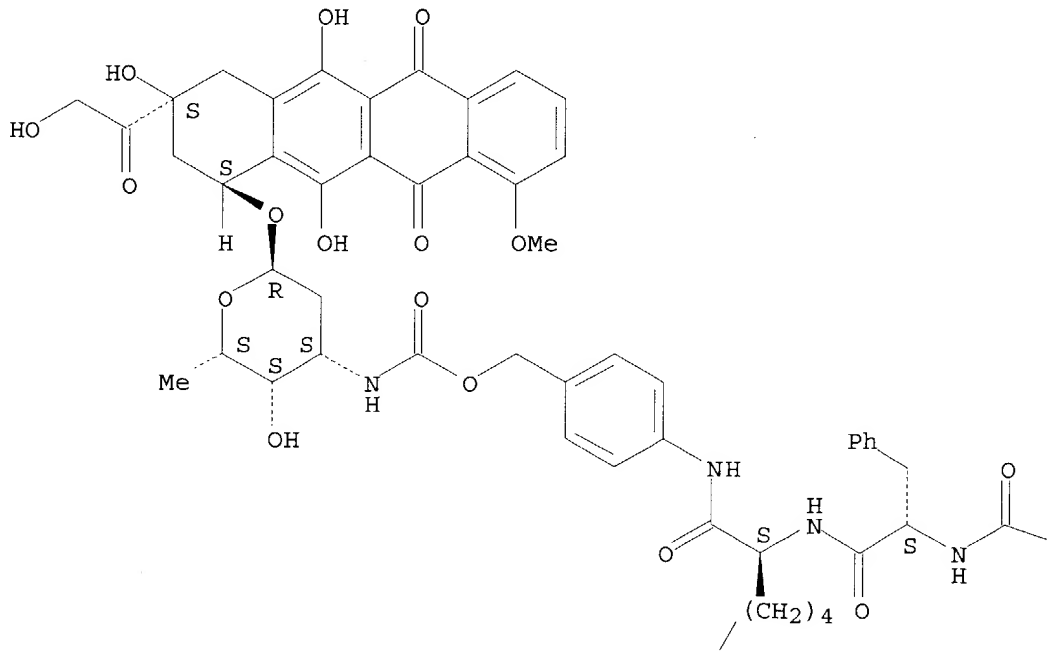
PAGE 3-B

RN 207613-83-0 HCAPLUS

CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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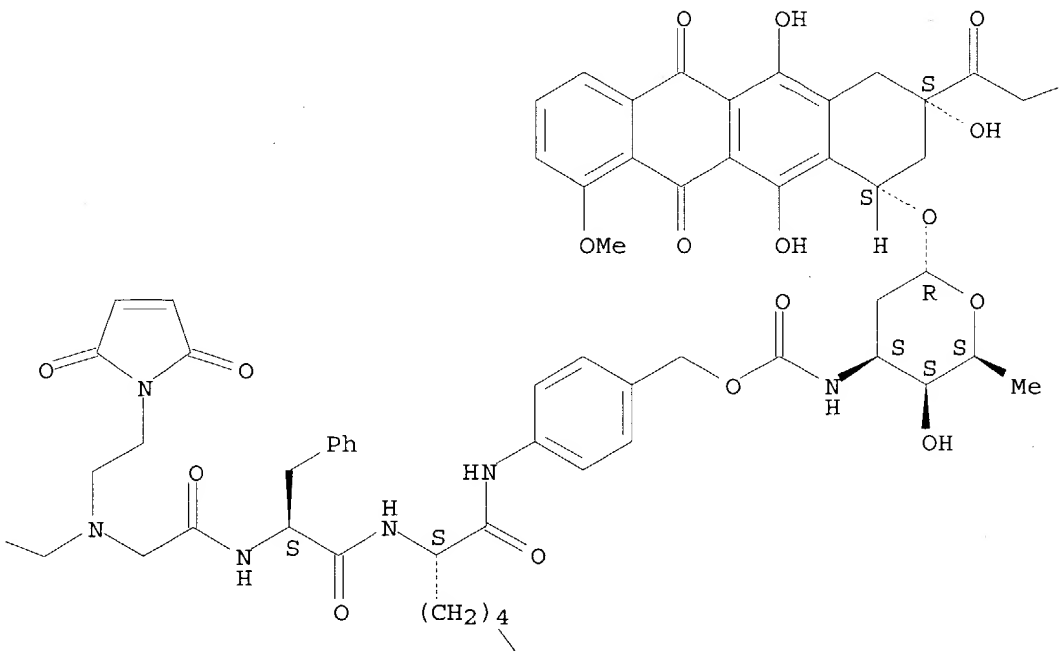

PAGE 1-C

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IT **207613-18-1P 207613-72-7P 499137-63-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antitumor activity of doxorubicin **conjugate** with monoclonal antibody BR96)

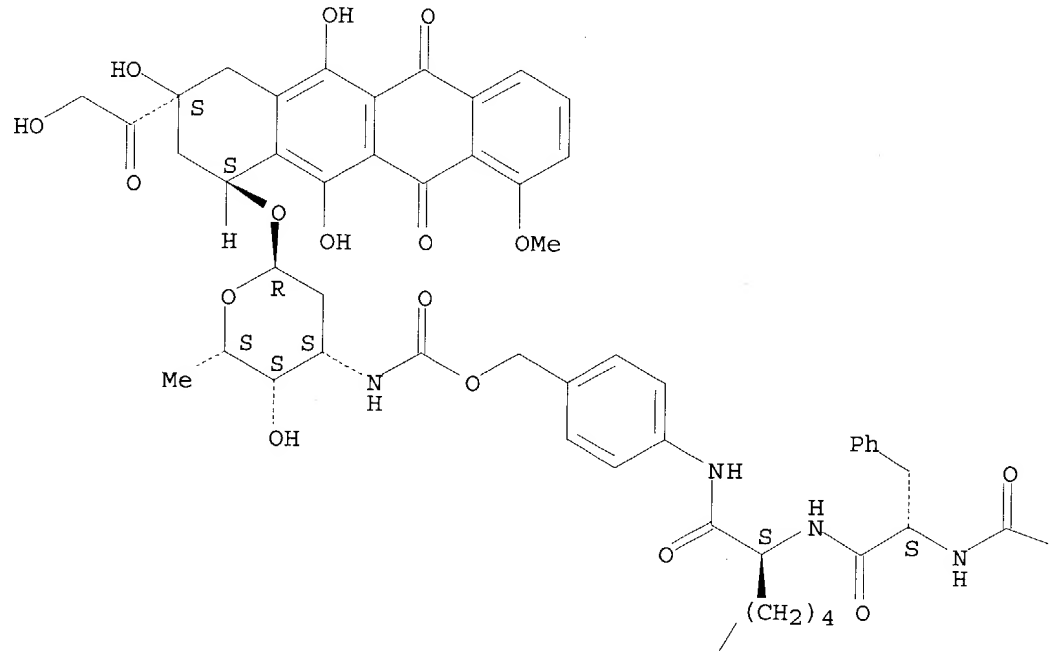
RN 207613-18-1 HCAPLUS

CN L-Lysinamide, N~(carboxymethyl)-N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-

1-methoxy-5,12-naphthacenedione, (1→1')-amide with
L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with
(8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-
hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-
1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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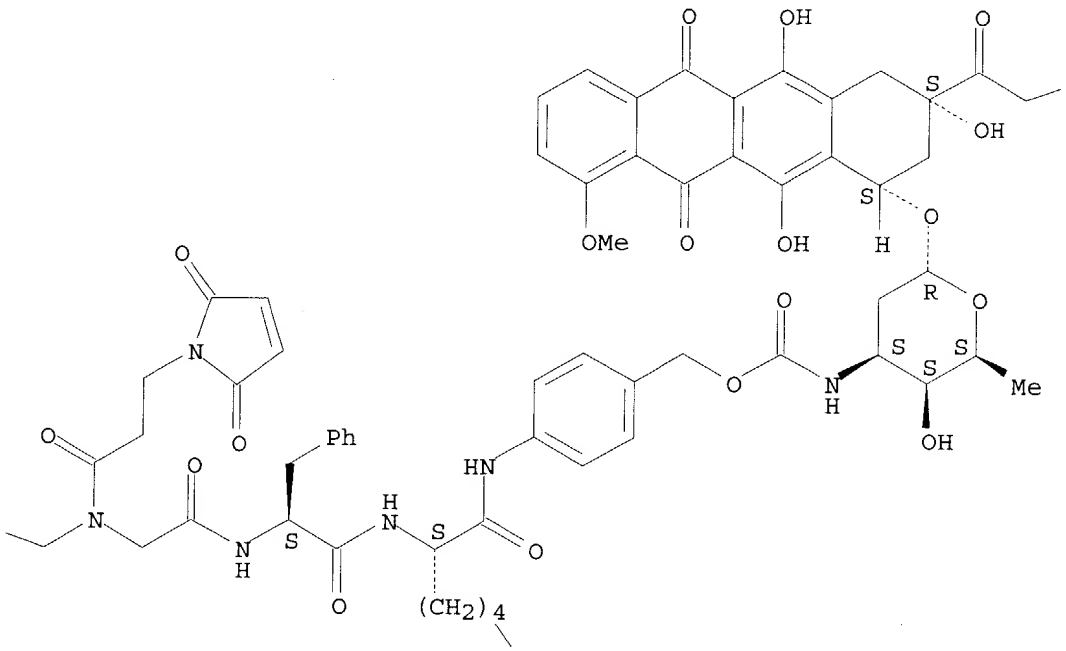

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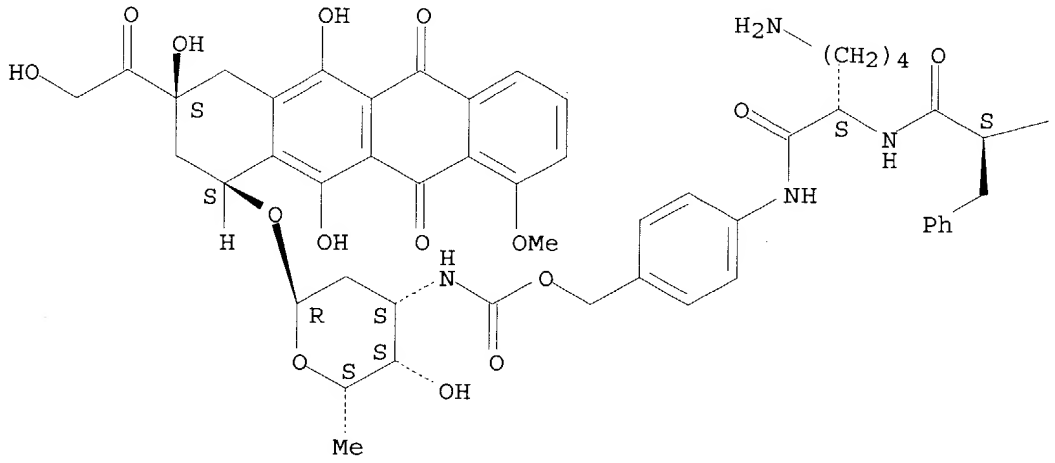
RN 207613-72-7 HCAPLUS

CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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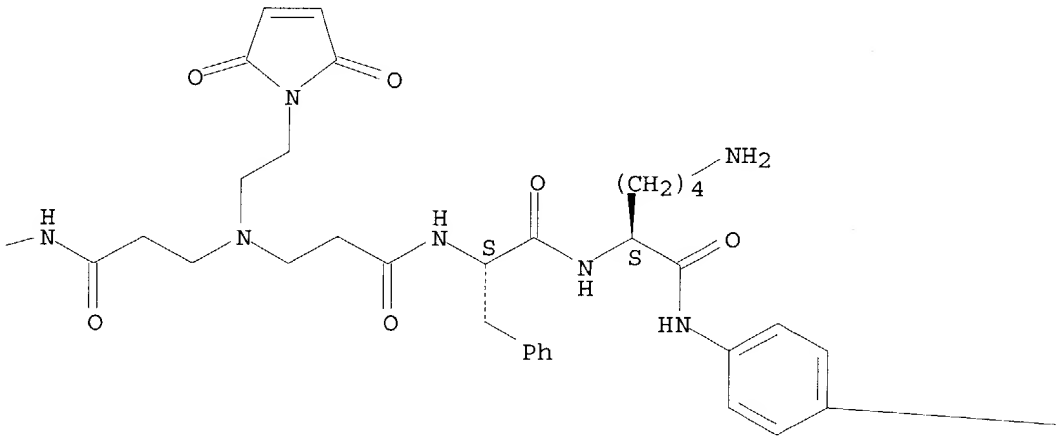

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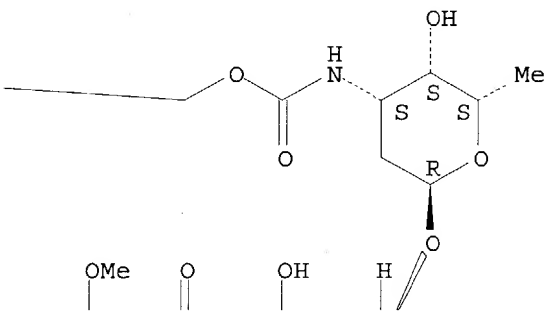

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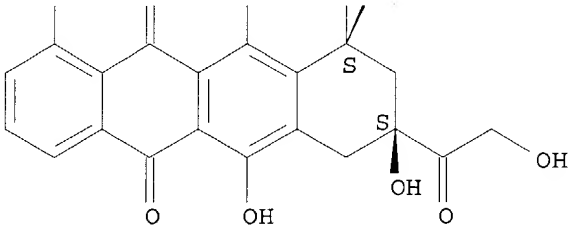

RN 499137-63-2 HCAPLUS
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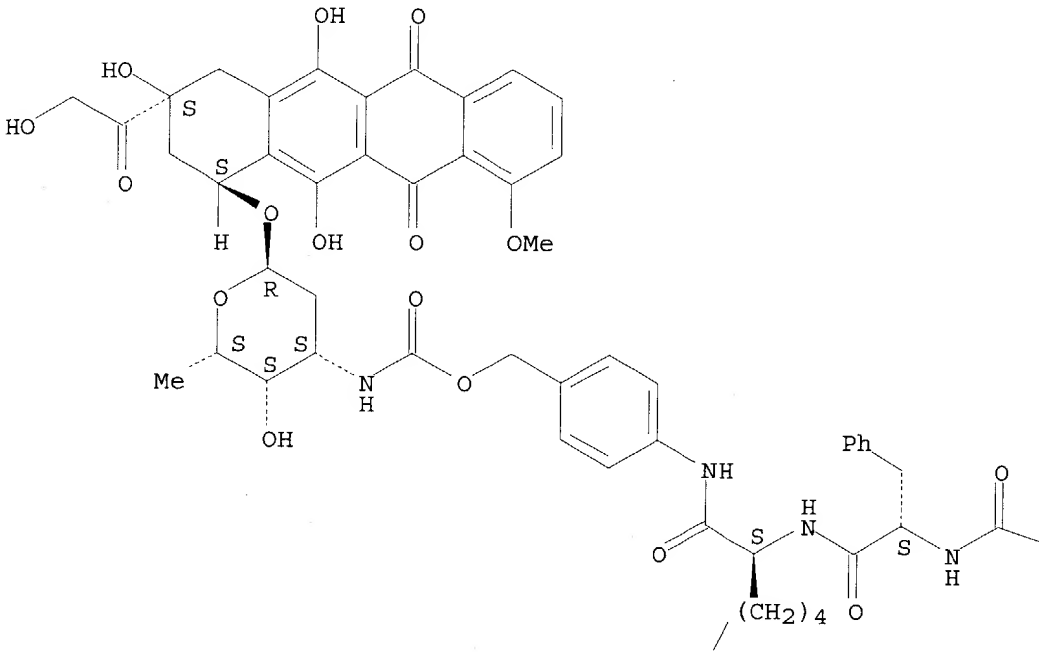
Absolute stereochemistry.

PAGE 1-A



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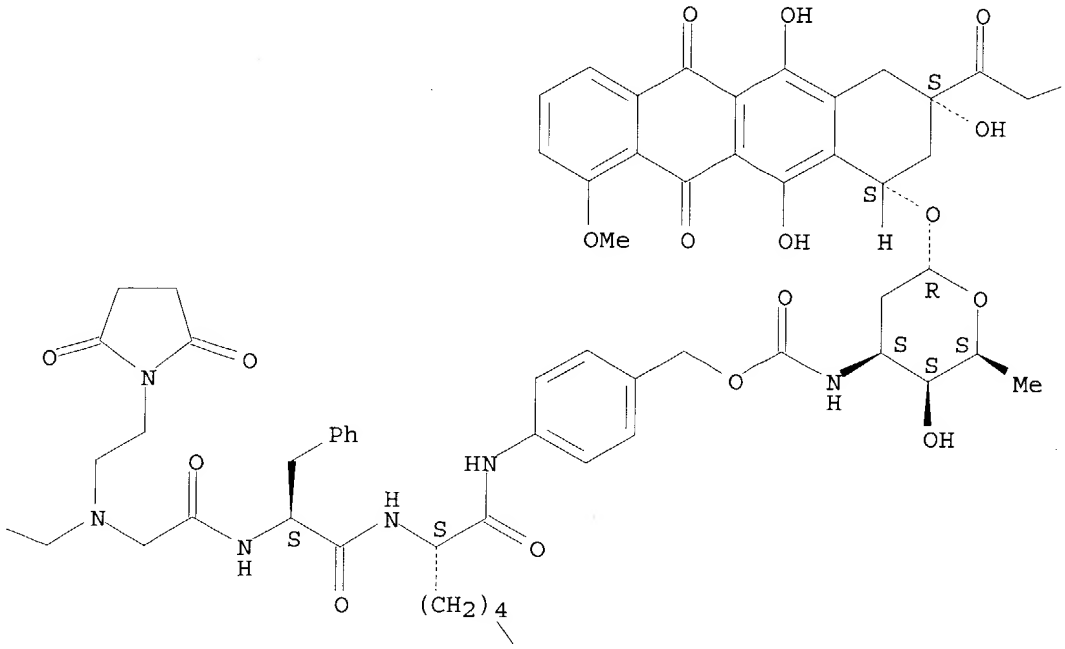

Searched by P. Ruppel

PAGE 1-C

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PAGE 2-B

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:1482 HCAPLUS
DOCUMENT NUMBER: 137:190500
TITLE: Synthesis of an immunoconjugate of camptothecin
AUTHOR(S): Walker, Michael A.; Dubowchik, Gene M.; Hofstead, Sandra J.; Trail, Pamela A.; Firestone, Raymond A.
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT, 06492, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(2), 217-219
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

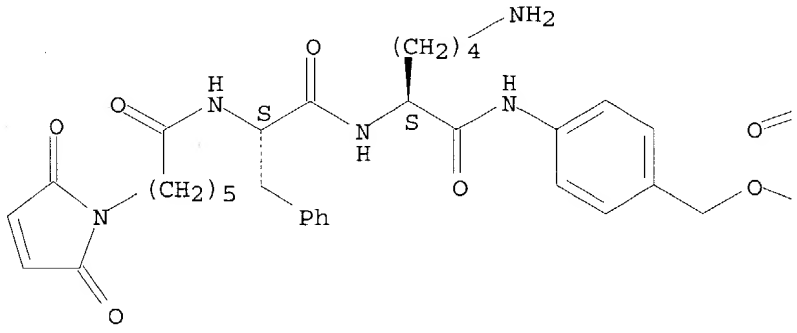
AB The first immunoconjugate of camptothecin has been synthesized wherein the drug is attached to the tumor-recognizing antibody BR96 via a Cathepsin B cleavable linker. Endocytosis of the immunoconjugate upon binding to the tumor cell followed by enzymic cleavage of the linker inside the endosome ensures tumor-specific release of the drug. In this way, it is hoped that the dose-limiting side effects associated with camptothecin can be eliminated while the antitumor activity is preserved.

IT **450366-26-4DP**, antibody **conjugate**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, stability and antitumor activity of camptothecin immunoconjugate)
RN 450366-26-4 HCAPLUS
CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-

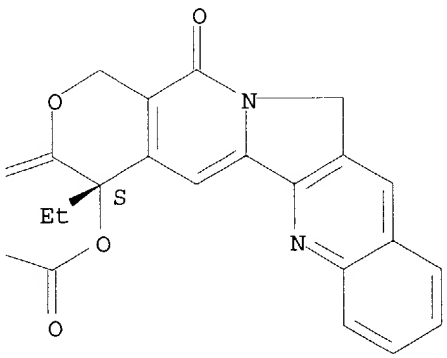
phenylalanyl-N-[4-[[[[[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



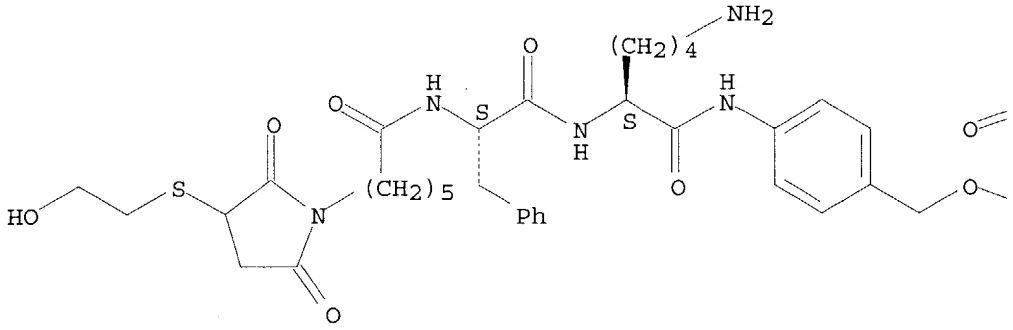
IT **450366-19-5P 450366-27-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, stability and antitumor activity of camptothecin immunoconjugate)

RN 450366-19-5 HCAPLUS

CN L-Lysinamide, N-[6-[3-[(2-hydroxyethyl)thio]-2,5-dioxo-1-pyrrolidinyl]-1-oxohexyl]-L-phenylalanyl-N-[4-[[[[[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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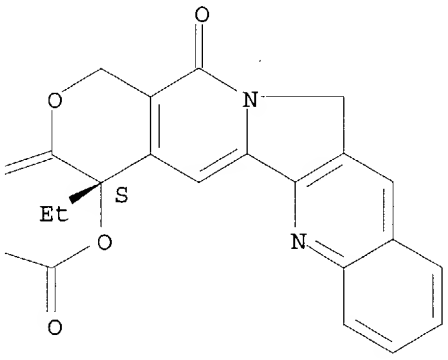


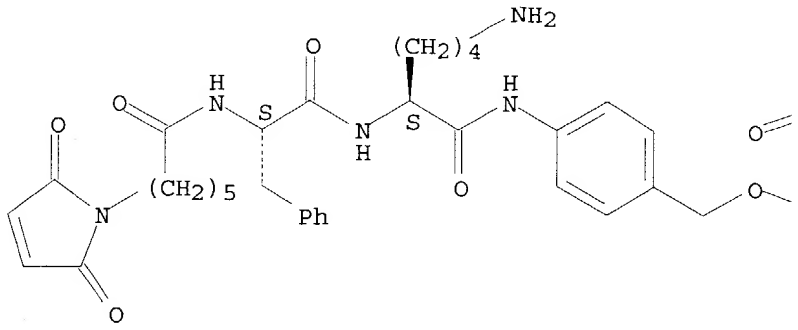
RN 450366-27-5 HCAPLUS
CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N-[4-[[[[[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]carbonyl]oxy]methyl]phenyl]-, mono(dichloroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 450366-26-4
CMF C53 H55 N7 O11

Absolute stereochemistry.

PAGE 1-A



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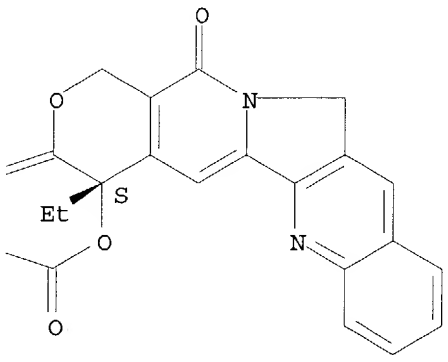

CM 2

CRN 79-43-6
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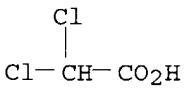


REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:635936 HCAPLUS
DOCUMENT NUMBER: 135:200481
TITLE: Caspase-activated prodrugs therapy
INVENTOR(S): Carter, Paul J.; Gazzard, Lewis
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062300	A2	20010830	WO 2001-US5709	20010222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1257296	A2	20021120	EP 2001-912935	20010222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001008930	A	20021210	BR 2001-8930	20010222
JP 2003523407	T2	20030805	JP 2001-561363	20010222
ZA 2002006105	A	20030731	ZA 2002-6105	20020731
US 2004052793	A1	20040318	US 2002-182975	20020802

PRIORITY APPLN. INFO.: US 2000-184779P P 20000224
WO 2001-US5709 W 20010222

AB The invention provides novel methods for the localized delivery of pharmaceutical agents by the administration of a caspase conjugate that targets a cell type of interest, i.e., tumor cells, and the addnl. administration of a pro-agent that is locally converted, in the presence of the caspase, to an active agent. The invention further provides novel targeting agents comprising a caspase as well as novel prodrugs comprising a caspase cleavable prodrug moiety. The invention also provides pharmaceutical compns. as well as methods of treatment comprising the caspase conjugates and prodrugs of the invention. For example, the peptide-doxorubicin conjugate, Ac-DEVD-PABC-doxorubicin (preparation given), was found to be more than 100-fold less toxic than doxorubicin against breast carcinoma cell lines. However, Ac-DEVD-PABC-doxorubicin was equally toxic to doxorubicin following treatment with caspase 3 due to efficient activation by the enzyme.

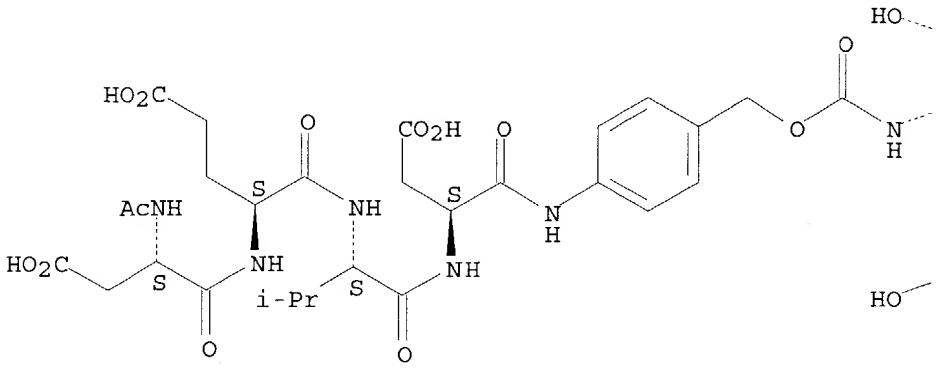
IT **357165-32-3P 357165-34-5P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(caspase-activated prodrugs for cancer therapy)

RN 357165-32-3 HCAPLUS

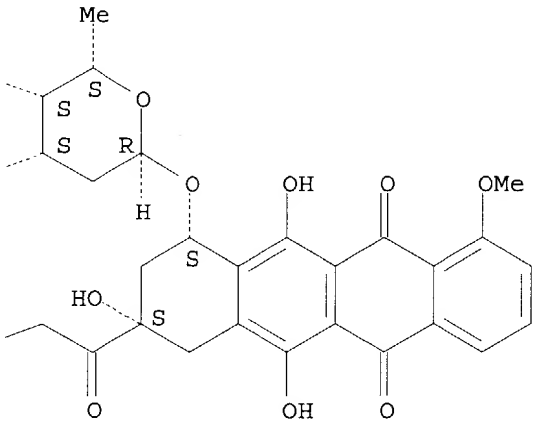
CN 5,12-Naphthacenedione, 10-[[3-[[[[4-[(N-acetyl-L-α-aspartyl-L-α-glutamyl-L-valyl-L-α-aspartyl)amino]phenyl]methoxy]carbonyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

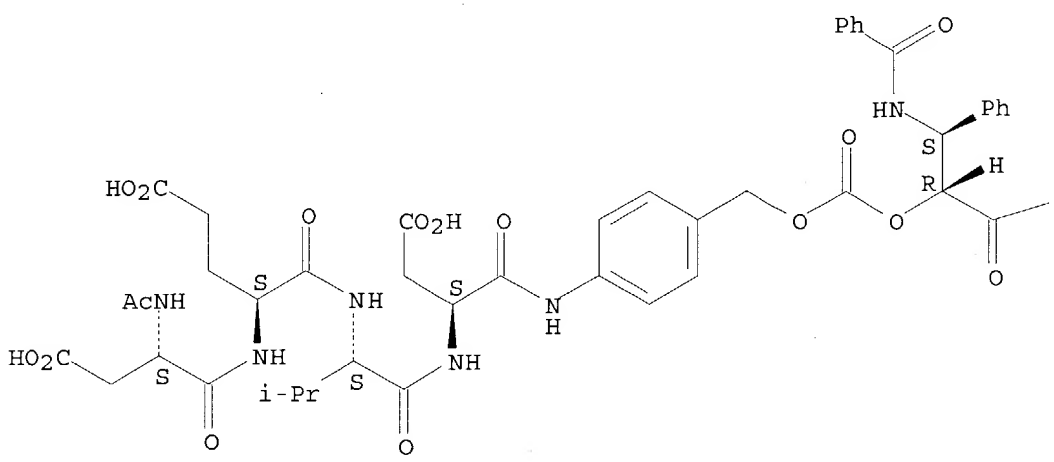


RN 357165-34-5 HCAPLUS

CN L-α-Asparagine, N-acetyl-L-α-aspartyl-L-α-glutamyl-L-valyl-N-[4-[[[[(1R,2S)-2-(benzoylamino)-1-[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy]carbonyl]-2-phenylethoxy]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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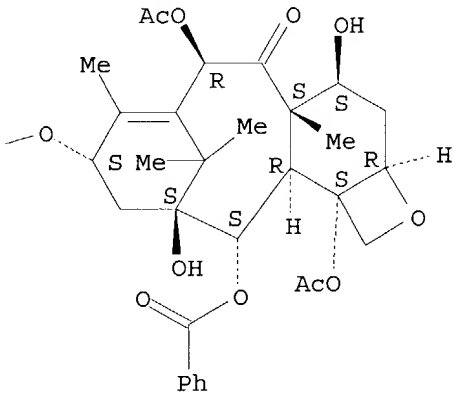


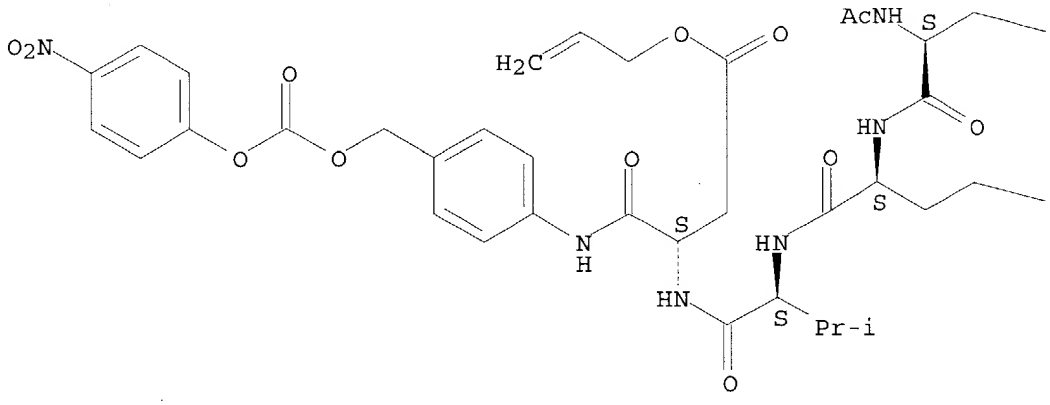
IT **357165-30-1P 357165-31-2P 357165-33-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(caspase-activated prodrugs for cancer therapy)

RN 357165-30-1 HCAPLUS

CN L-α-Asparagine, N-acetyl-L-α-aspartyl-L-α-glutamyl-L-valyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-, tri-2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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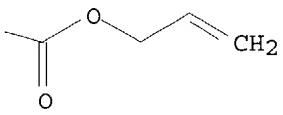

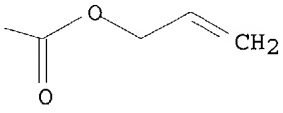

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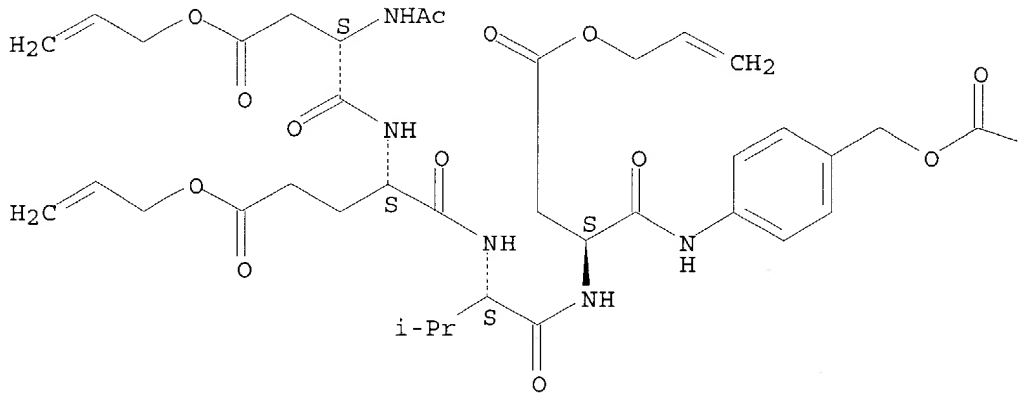
CN 5,12-Naphthacenedione, 10-[[3-[[[[4-[(N-acetyl-L-α-aspartyl-L-α-glutamyl-L-valyl-L-α-asparty1)amino]phenyl]methoxy]carbonyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, tri-2-propenyl ester, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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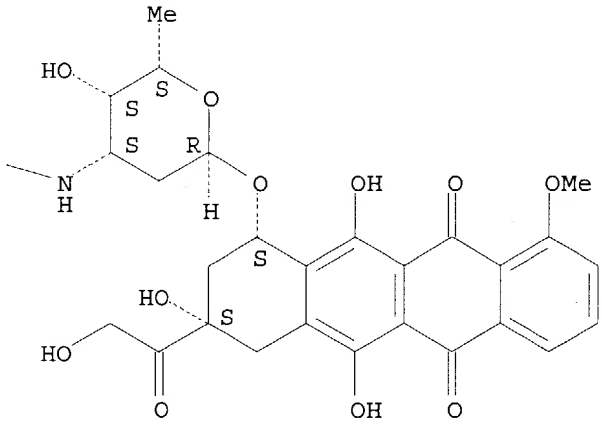
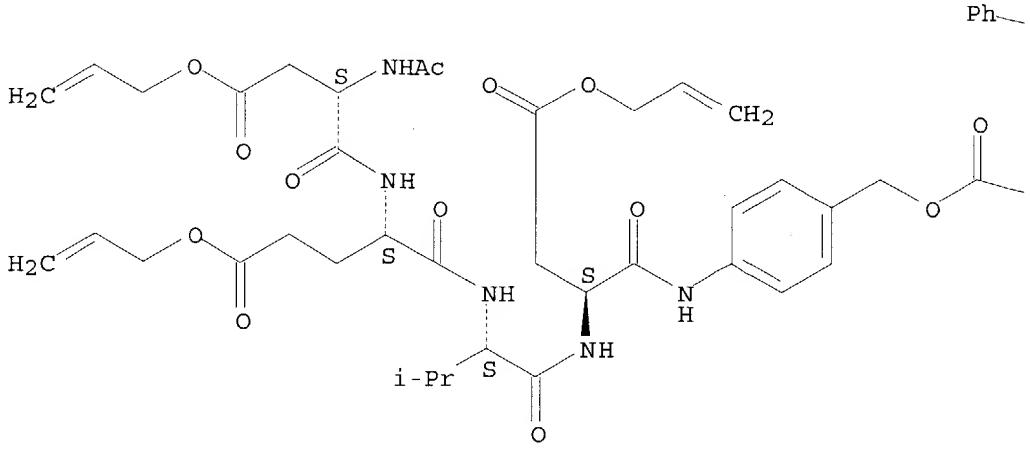


RN 357165-33-4 HCAPLUS

CN L-α-Asparagine, N-acetyl-L-α-aspartyl-L-α-glutamyl-L-valyl-N-[4-[[[[(1R,2S)-2-(benzoylamino)-1-[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy]carbonyl]-2-phenylethoxy]carbonyl]oxy]methyl]phenyl]-, tri-2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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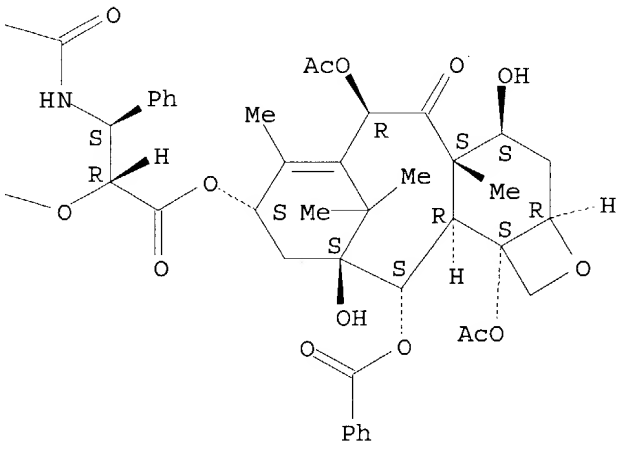


L9 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:763905 HCAPLUS
DOCUMENT NUMBER: 132:15631
TITLE: Antitumor or antiinflammatory drug composites
INVENTOR(S): Susaki, Hiroshi; Inoue, Kazuhiro; Kuga, Hiroshi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961061	A1	19991202	WO 1999-JP2681	19990521

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,

DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2333321	AA	19991202	CA 1999-2333321		19990521
AU 9937333	A1	19991213	AU 1999-37333		19990521
EP 1080732	A1	20010307	EP 1999-919664		19990521
R: BE, CH, DE, FR, GB, IT, LI, NL, SE					
NO 2000005913	A	20010122	NO 2000-5913		20001122
PRIORITY APPLN. INFO.:			JP 1998-140915	A	19980522
			WO 1999-JP2681	W	19990521

AB Drug composites useful as DDS compds., which are represented by the general formula: A-R-NH-Y-CH2-O-CO-Q (wherein A is a polymer serving as a carrier for a drug; R is a spacer comprising one amino acid mol. or one comprising 2 to 8 amino acid mols. bound to each other through peptide linkage; Y is optionally substituted phenylene; and Q is a residue of a drug compound such as an antitumor agent). The composites permit the speedy and regioselective release of drug compds. such as antitumor or anti-inflammatory agents, thus exhibiting expected drug effects without fail. A composite of DX-8951 [(1S,9S)-1-Amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-10,13(9H,15H)-dione] was prepared from DX-8951 methanesulfonic acid salt, dextran polyalc. Na salt, Boc-Gly-Gly-Phe-Gly-OH, 4-aminobenzylalc., and bis(4-nitrophenyl)carbonate.

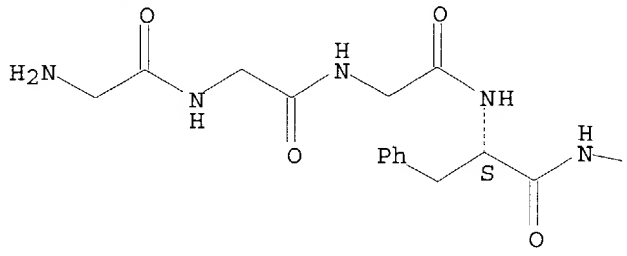
IT **251459-40-2DP**, reaction products with **dextran** and acetic acid **251459-41-3DP**, reaction products with **dextran** and acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor or antiinflammatory drug **dextran polyalc**. **conjugates**)

RN 251459-40-2 HCAPLUS

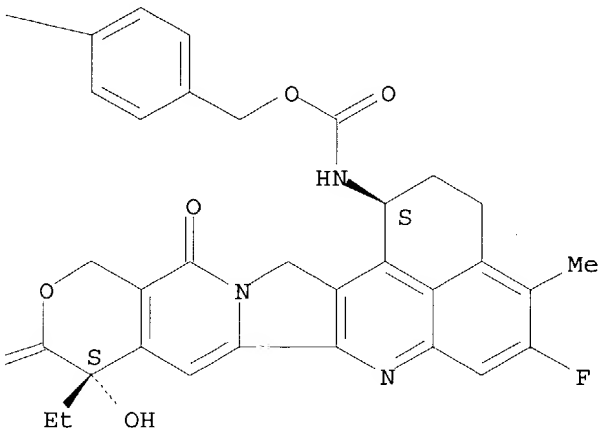
CN L-Phenylalaninamide, glycylglycylglycyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

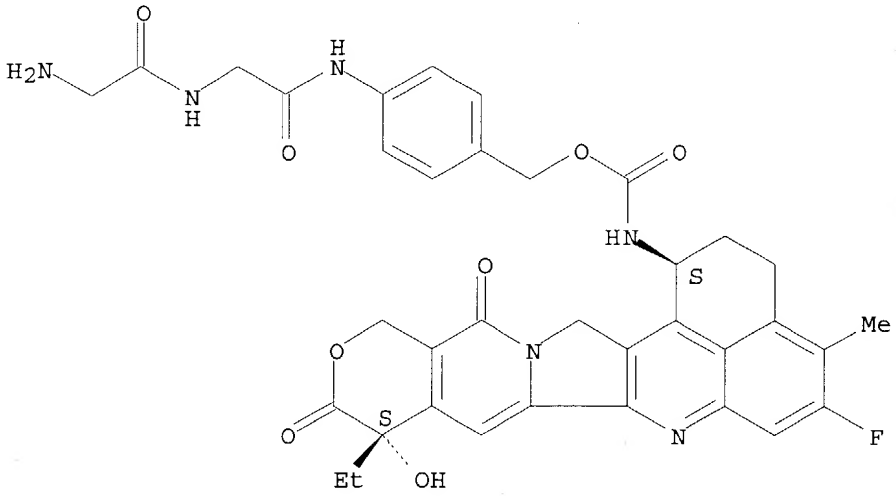


PAGE 1-B



RN 251459-41-3 HCAPLUS
CN Glycinamide, glycyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

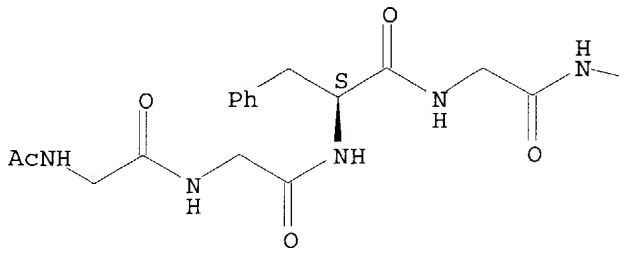
Absolute stereochemistry.



IT **251459-33-3DP**, reaction products with **dextran** and acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor or antiinflammatory drug **dextran polyalc. conjugates**)
RN 251459-33-3 HCAPLUS
CN Glycinamide, N-acetylglycylglycyl-L-phenylalanyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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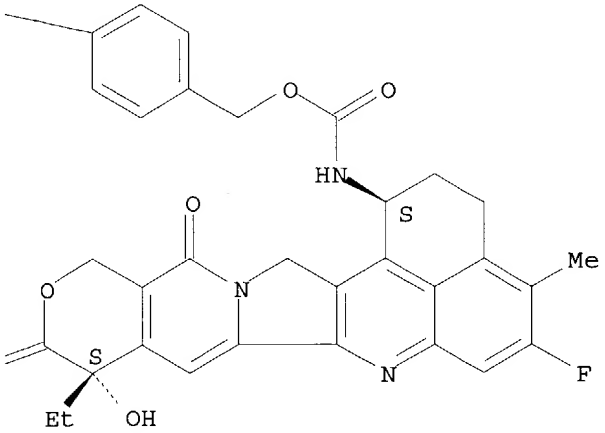


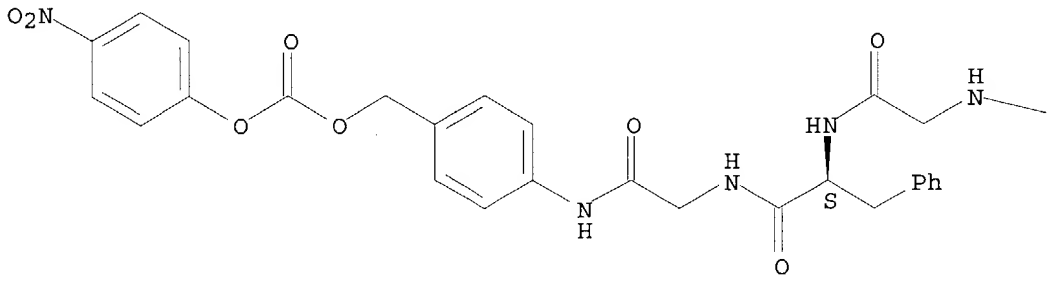
IT **251459-29-7P 251459-31-1P 251459-32-2P**
251459-36-6P 251459-37-7P 251459-38-8P
251459-39-9P 251459-40-2DP, reaction products with **dextran** and acetic acid **251459-41-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor or antiinflammatory drug **dextran polyalc. conjugates**)

RN 251459-29-7 HCAPLUS

CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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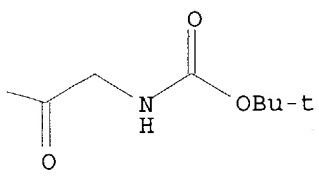
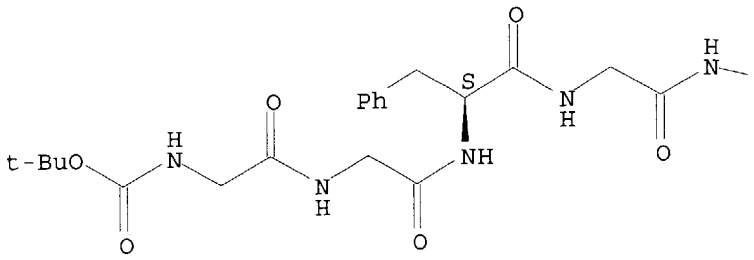


RN 251459-31-1 HCAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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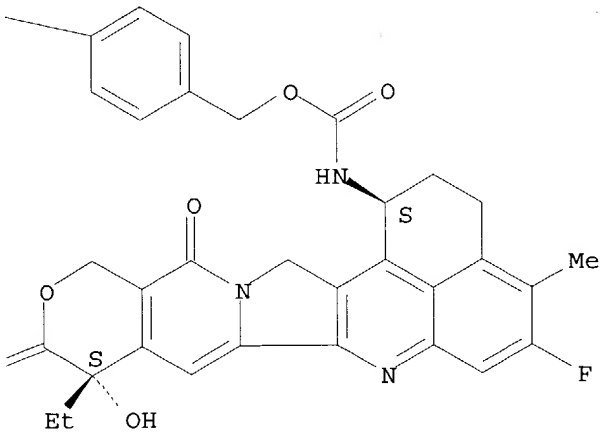

RN 251459-32-2 HCAPLUS
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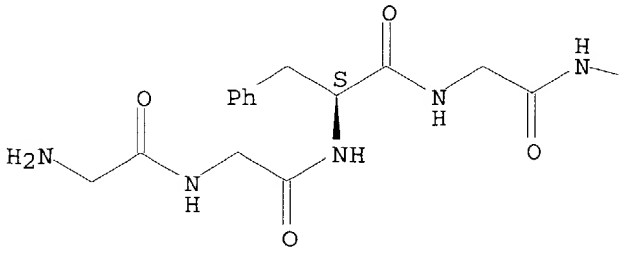
Absolute stereochemistry.

PAGE 1-A



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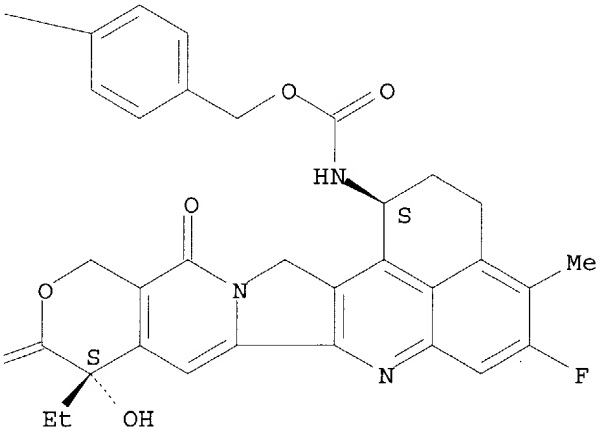

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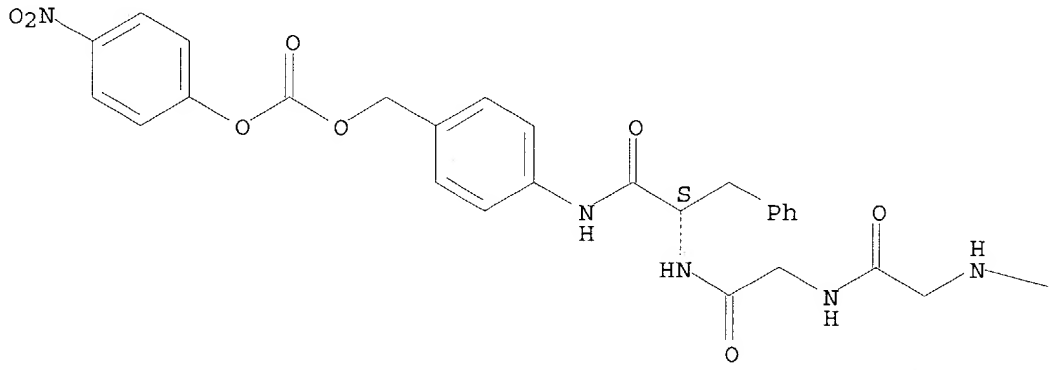
Absolute stereochemistry.

PAGE 1-A



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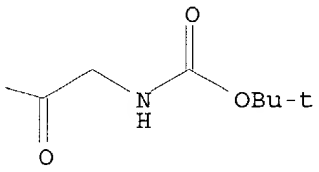

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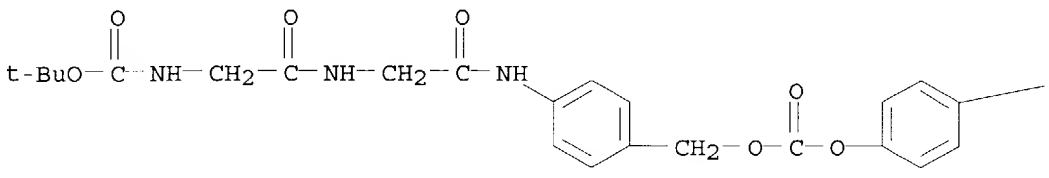
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

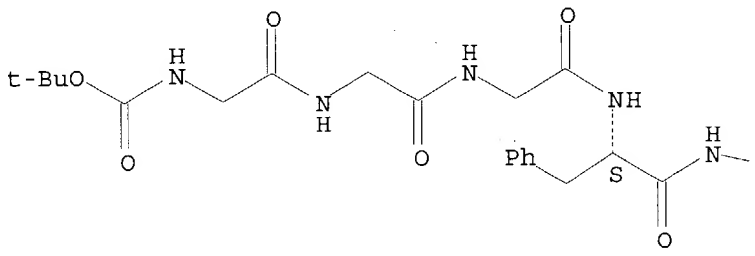


PAGE 1-B

RN 251459-38-8 HCAPLUS
CN L-Phenylalaninamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycylglycyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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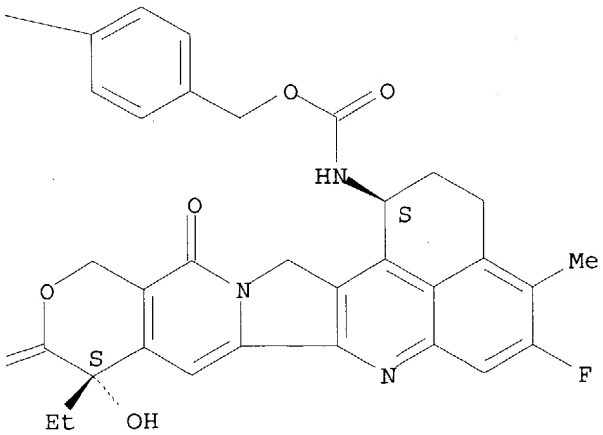
PAGE 1-B



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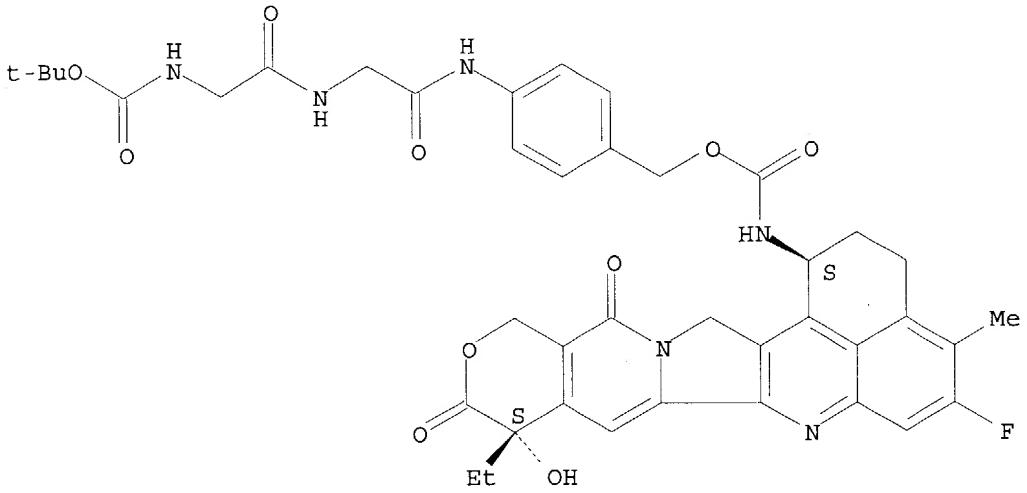
Absolute stereochemistry.



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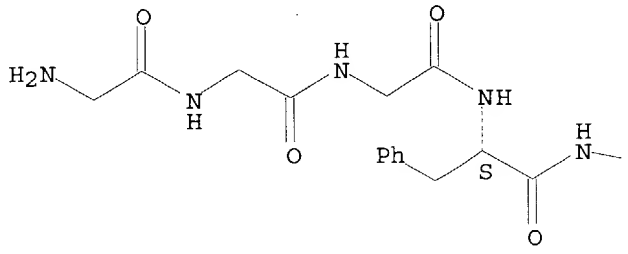
Absolute stereochemistry.

PAGE 1-A



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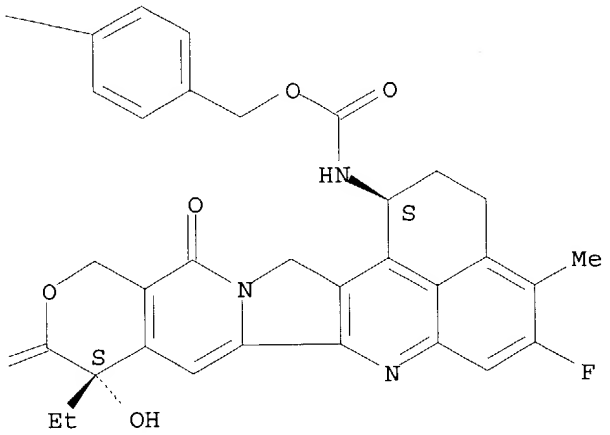

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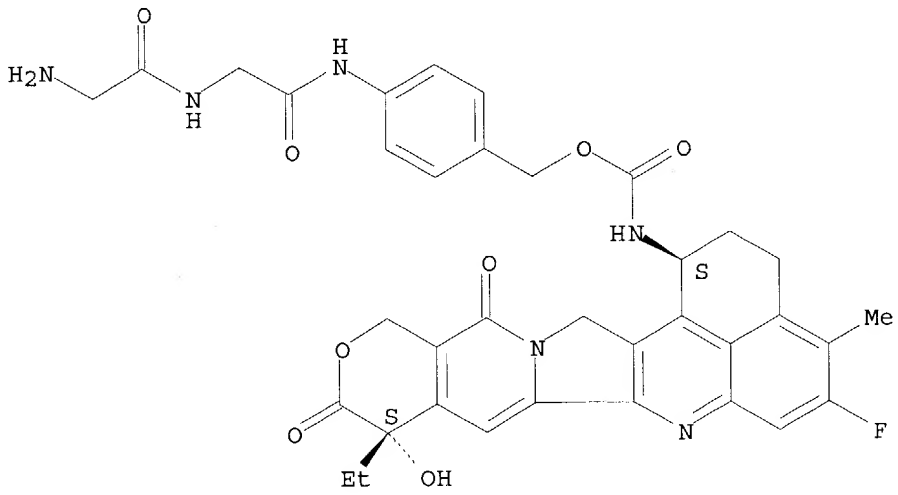
Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:323158 HCAPLUS
DOCUMENT NUMBER: 129:16386
TITLE: Preparation of branched peptide linkers

Searched by P. Ruppel

INVENTOR(S): King, Dalton; Firestone, Raymond A.; Dubowchik, Gene M.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819705	A1	19980514	WO 1997-US19851	19971031
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851597	A1	19980529	AU 1998-51597	19971031
EP 941120	A1	19990915	EP 1997-946428	19971031
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001505194	T2	20010417	JP 1998-521606	19971031

PRIORITY APPLN. INFO.: US 1996-30367P P 19961105
WO 1997-US19851 W 19971031

OTHER SOURCE(S): MARPAT 129:16386

AB Conjugates containing a targeting ligand, such as an antibody, a therapeutically active drug and a branched peptide linker are given. The branched peptide linker contains two or more amino acid moieties that provide an enzyme cleavage site. The number of drugs capable of being bonded to the branched linkers varies by a factor of two for each generation of branching. Compds. A-Wc-(CH2)a-(Q)p-(CO)d-E[(CH2)b-X]2 (A = thiol acceptor, W = bridging moiety, c = integer 0-1, a = 2-12, Q = O, NH, alkylimino, p, d = 0-1, E = polyvalent atom, b = 1-10, X = CO-Y-Zm-Gn, where Y = two L-amino acid residues, m = 0-1, G = self-immolative spacer, n = 0-1), and related compds. with further branching at X, are claimed. Thus, syntheses of MEt-IDP-[AA-Lys-PABC-DOX]2 dichloroacetates [MEt-IDP = N-maleoyl-N',N'-bis(carboxyethyl)ethylenediamine residue; AA = Lys, Phe, or Ala; PABC = p-NHC6H4CH2O2C; DOX = doxorubicin residue] are described.

IT **207612-97-3P 207613-09-0P 207613-10-3P**
207613-16-9P 207613-17-0P 207613-29-4P
207613-30-7P 207613-36-3P 207613-37-4P
207613-48-7P 207613-49-8P 207613-56-7P
207613-57-8P 207613-64-7P 207613-65-8P
207613-66-9P 207613-79-4P 207613-80-7P
207613-81-8P 207613-82-9P 207613-83-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of branched peptide linkers)

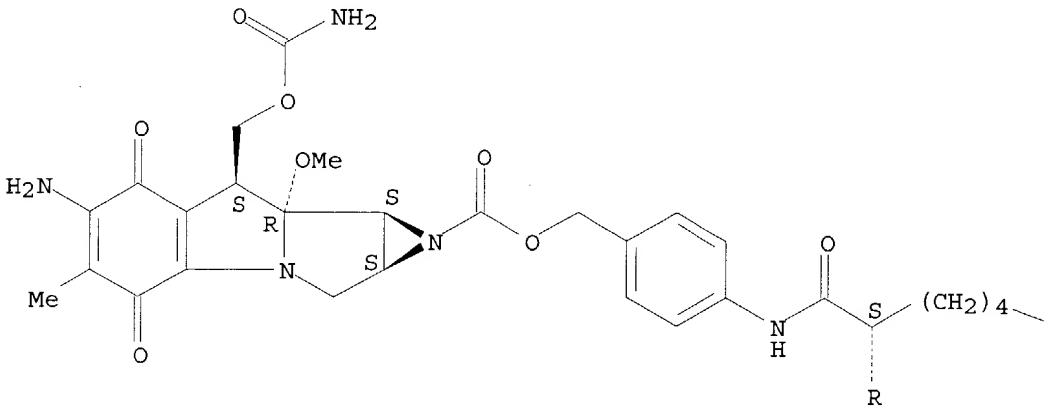
RN 207612-97-3 HCAPLUS

CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N-[4-[[[[(1aS,8S,8aR,8bS)-6-amino-8-[[(aminocarbonyl)oxy]methyl]-1a,4,7,8,8a,8b-hexahydro-8a-methoxy-5-methyl-4,7-dioxoazirino[2',3':3,4]pyrrolo[1,2-a]indol-1(2H)-yl]carbonyl]oxy]methyl]phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, (1→1')-amide with L-phenylalanyl-N-[4-[[[[(1aS,8S,8aR,8bS)-6-amino-8-[[(aminocarbonyl)oxy]methyl]-1a,4,7,8,8a,8b-hexahydro-8a-methoxy-5-

methyl-4,7-dioxoazirino[2',3':3,4]pyrrolo[1,2-a]indol-1(2H)-yl]carbonyl]oxy]methyl]phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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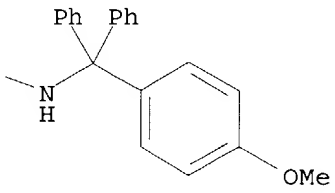

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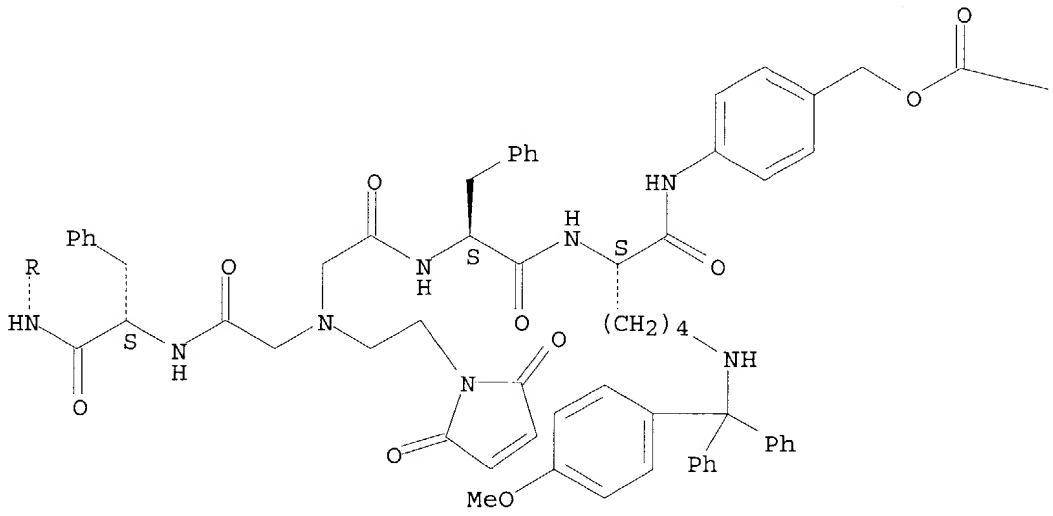

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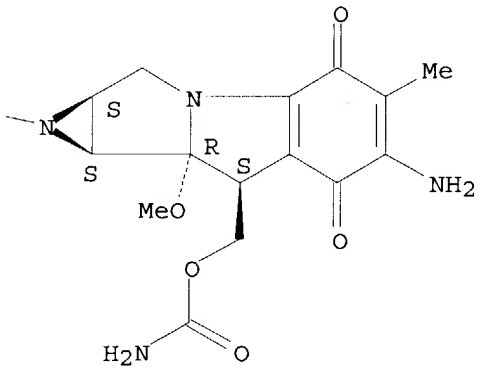
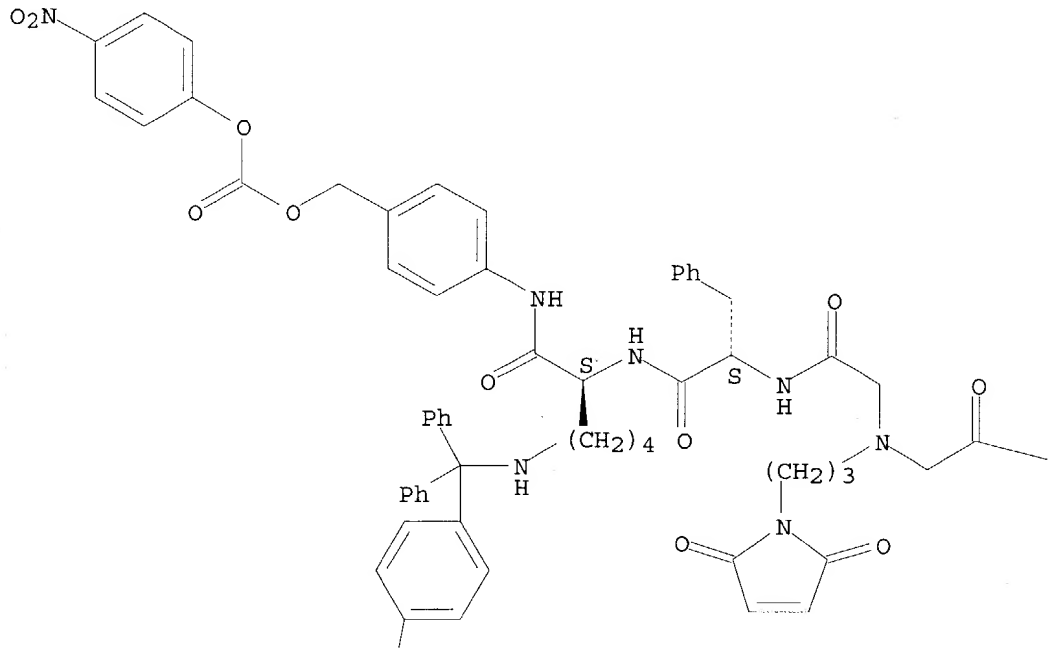


RN 207613-09-0 HCAPLUS

CN L-Lysinamide, N-(carboxymethyl)-N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]glycyl-L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-, (1→1')-amide with L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-L-lysinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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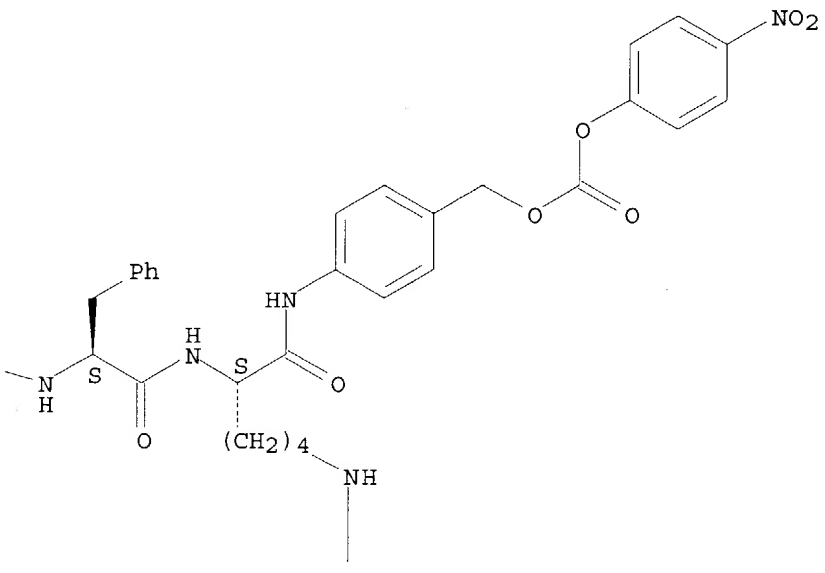
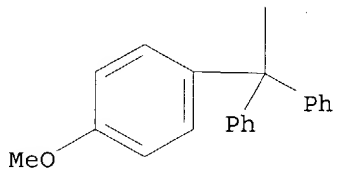


Searched by P. Ruppel

PAGE 2-A

PAGE 2-B

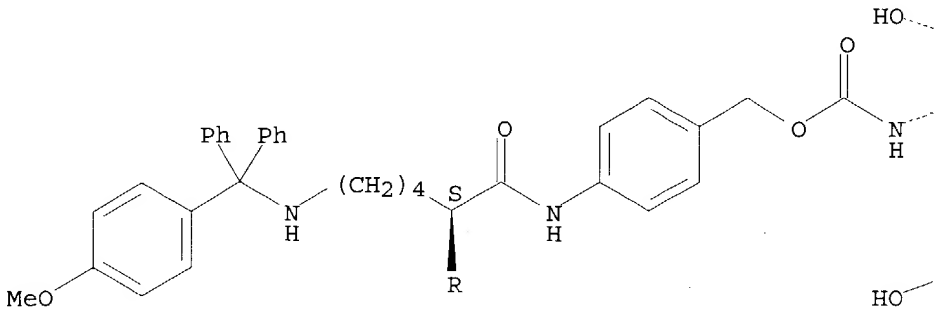


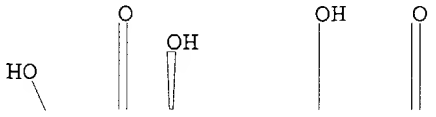
RN 207613-10-3 HCAPLUS

CN L-Lysinamide, N-(carboxymethyl)-N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





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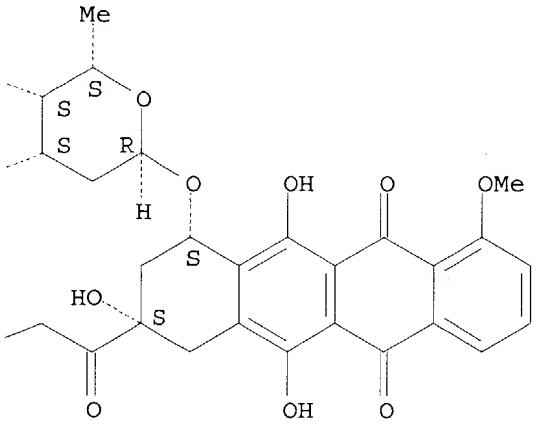

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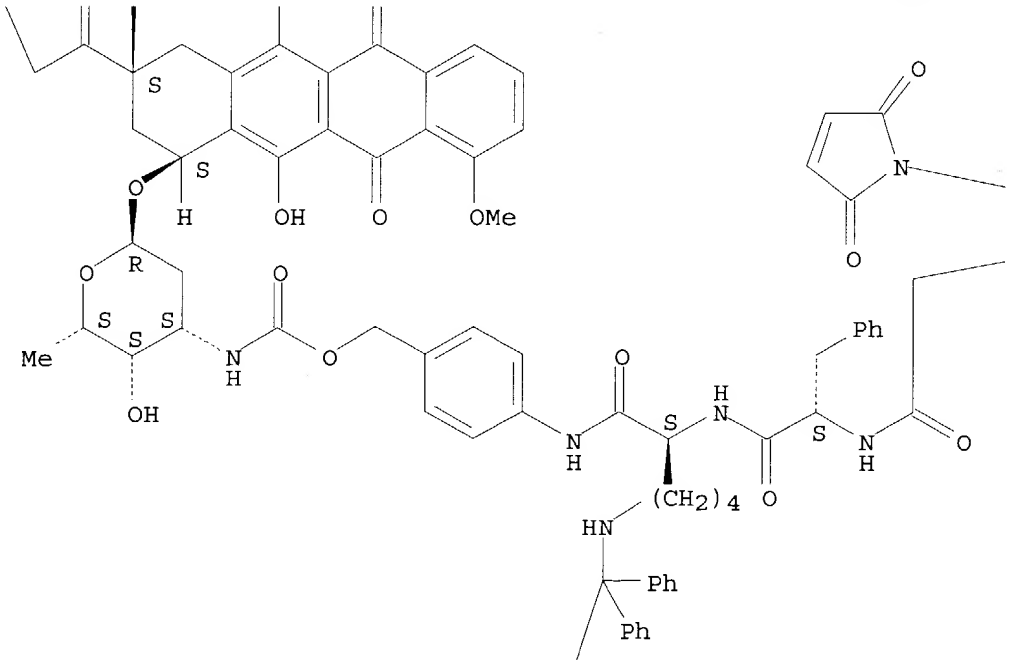

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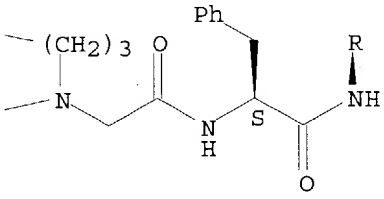

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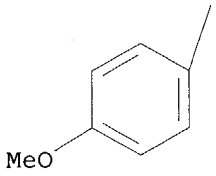

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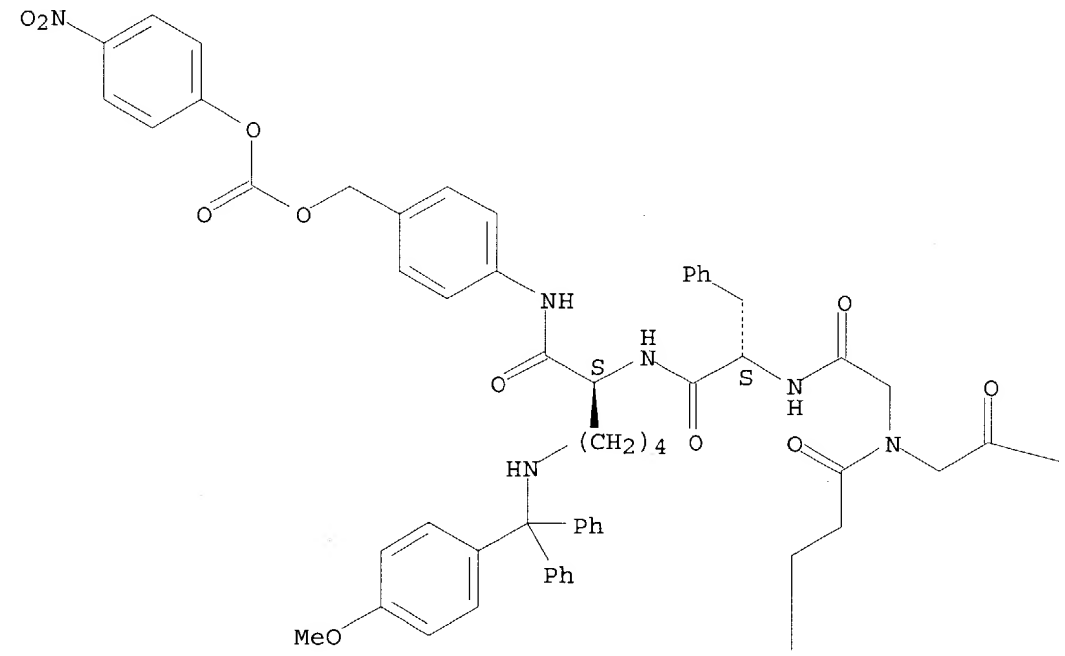
Absolute stereochemistry.

PAGE 1-A



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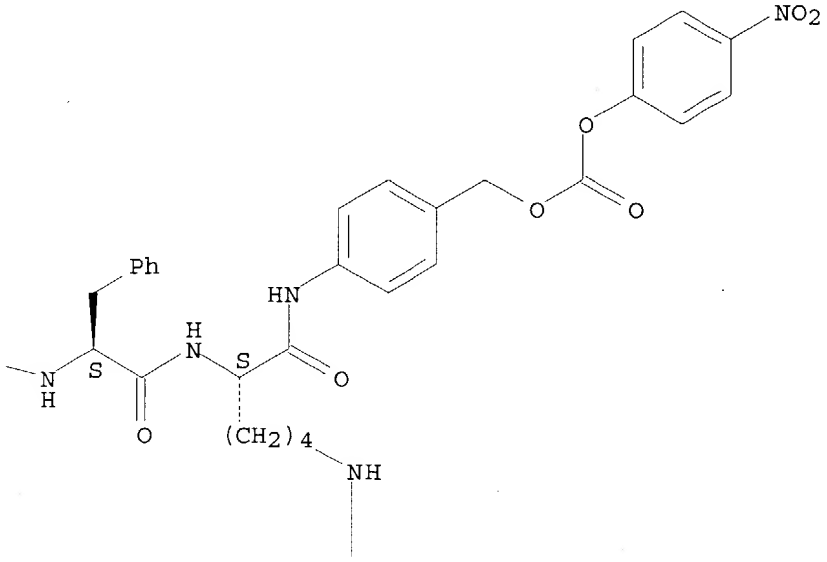

Searched by P. Ruppel

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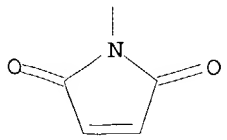

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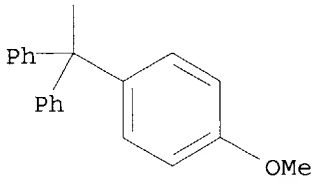

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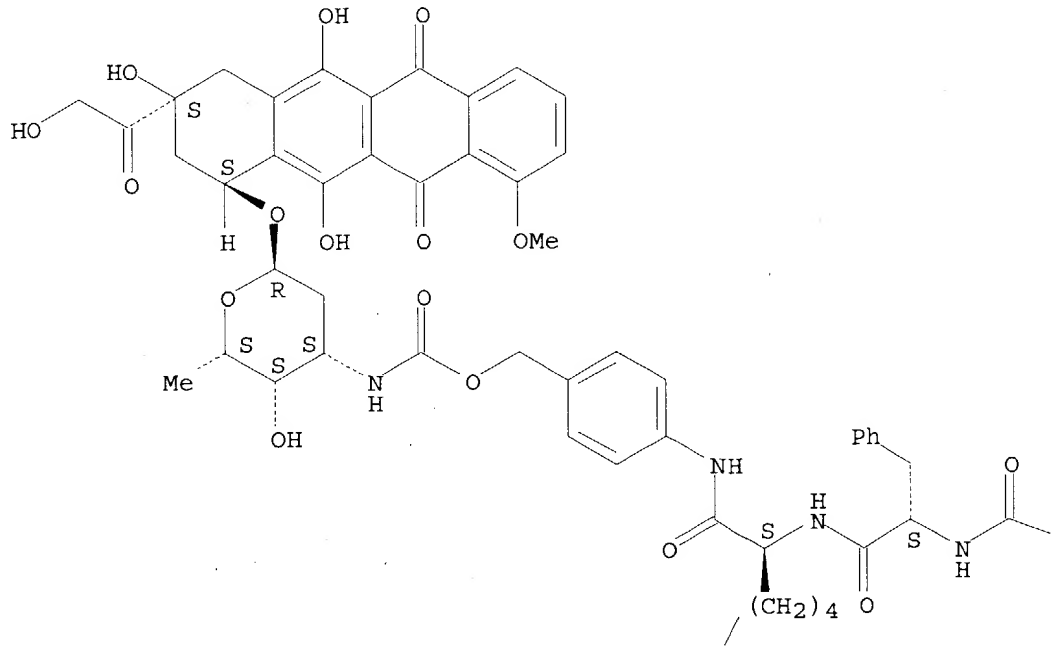
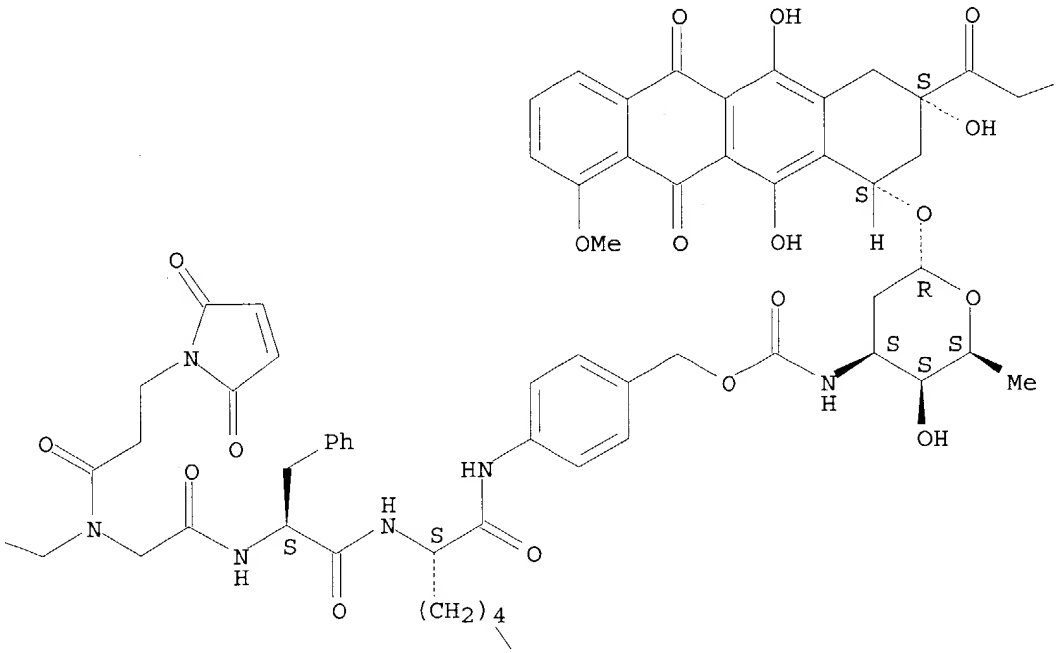
Absolute stereochemistry.

PAGE 1-A



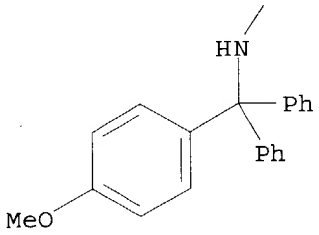
PAGE 1-B



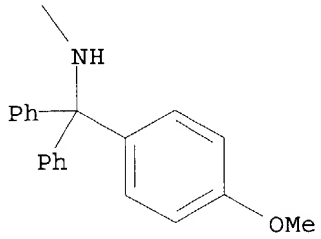
Searched by P. Ruppel

PAGE 1-C

PAGE 2-A



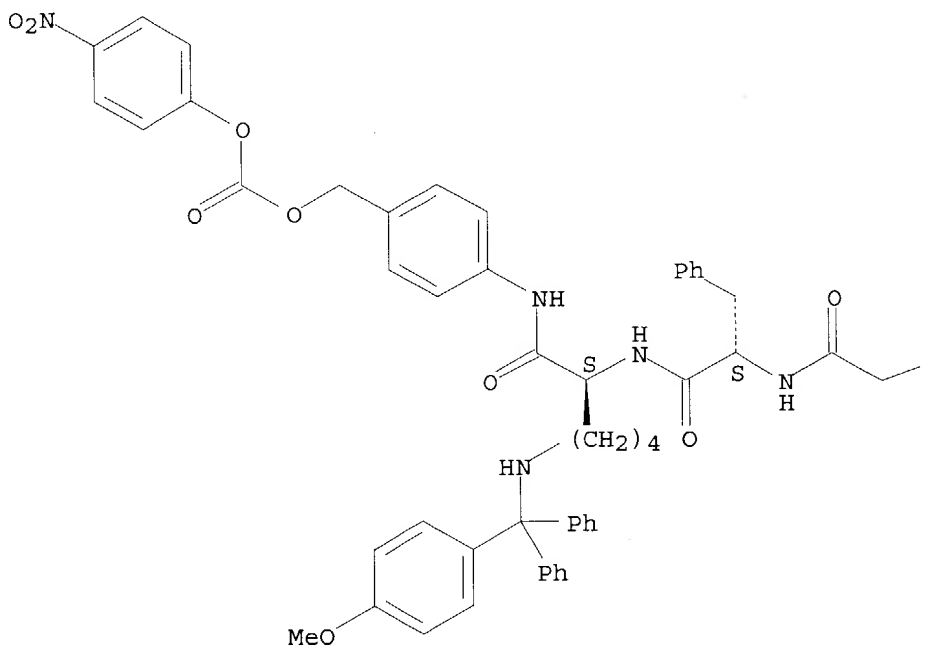
PAGE 2-B



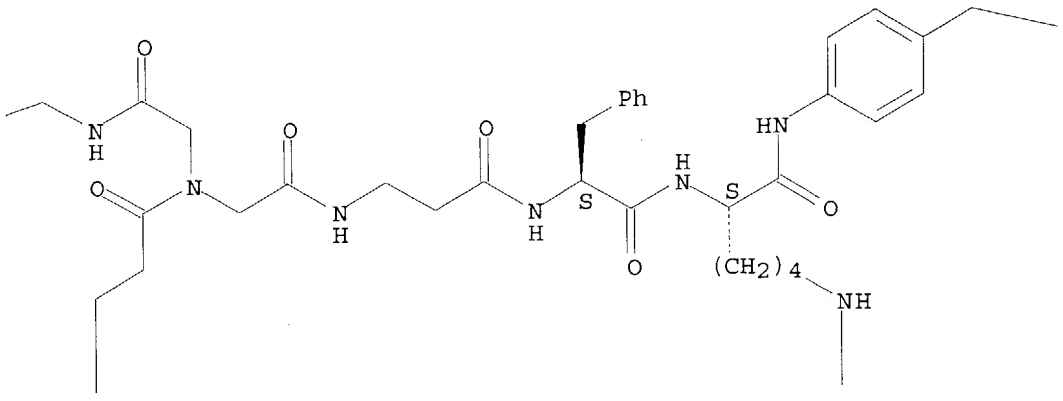
RN 207613-29-4 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]glycyl-β-alanyl-L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-, (1→1')-amide with β-alanyl-L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-L-lysinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

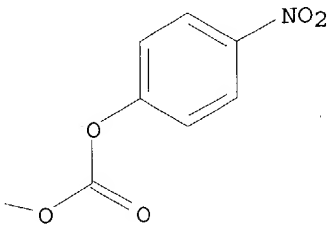


PAGE 1-B



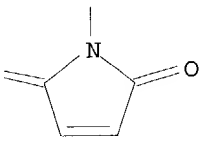
Searched by P. Ruppel

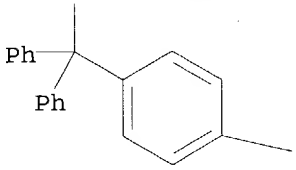
PAGE 1-C



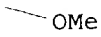
PAGE 2-A

PAGE 2-B





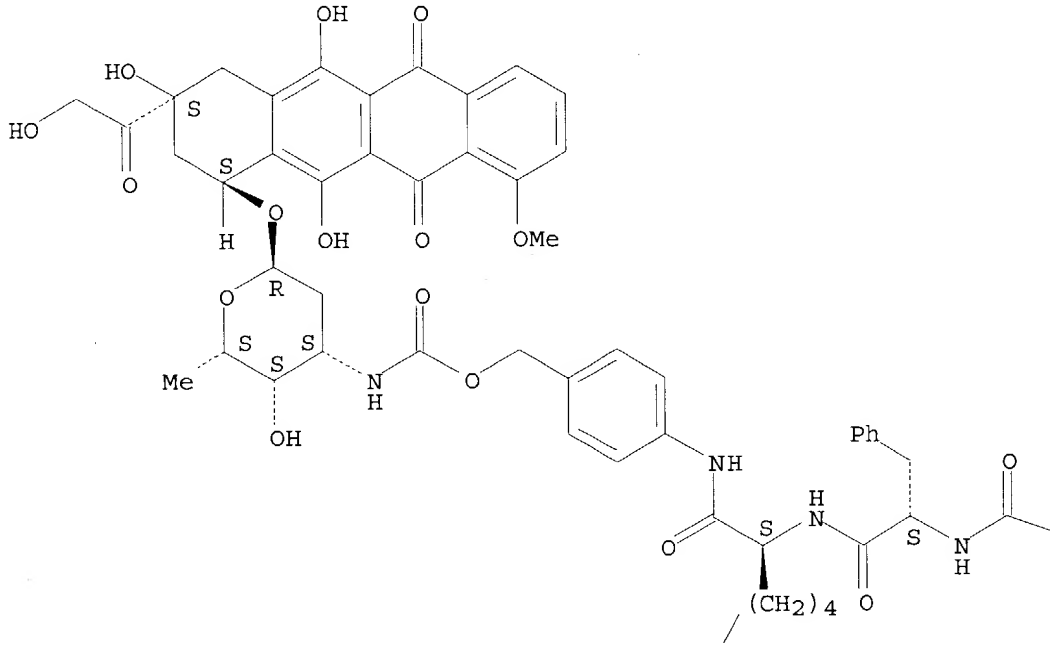
PAGE 2-C



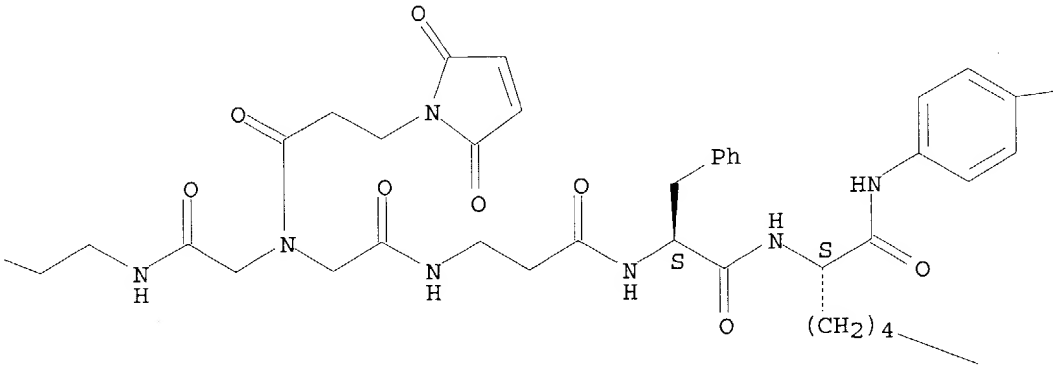
RN 207613-30-7 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]glycyl-β-alanyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, 4-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with β-alanyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

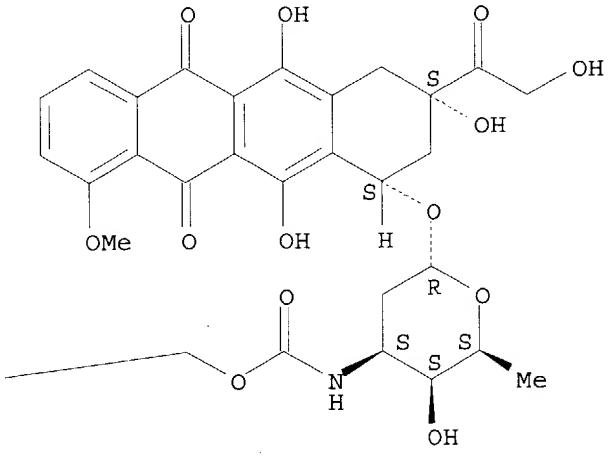


PAGE 1-B

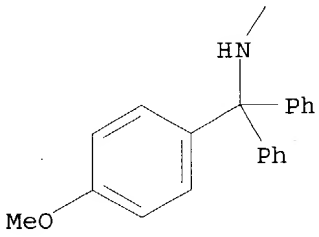


Searched by P. Ruppel

PAGE 1-C



PAGE 2-A



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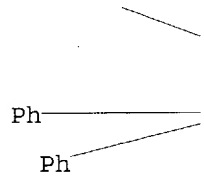
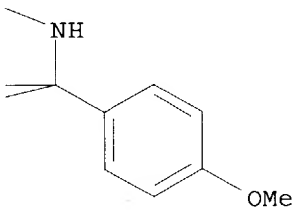


PAGE 2-C

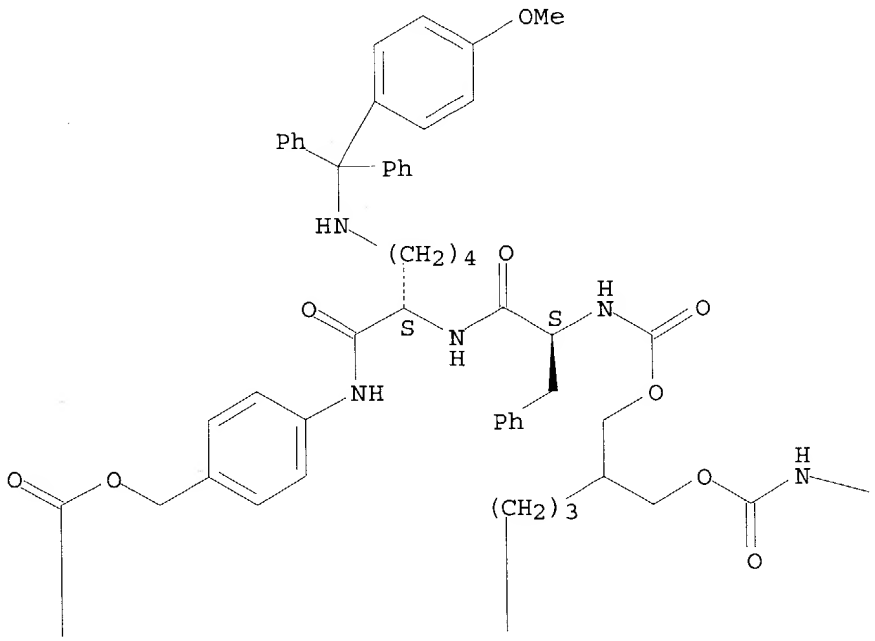


RN 207613-36-3 HCAPLUS
CN L-Lysinamide, 1,1'-[[2-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]-

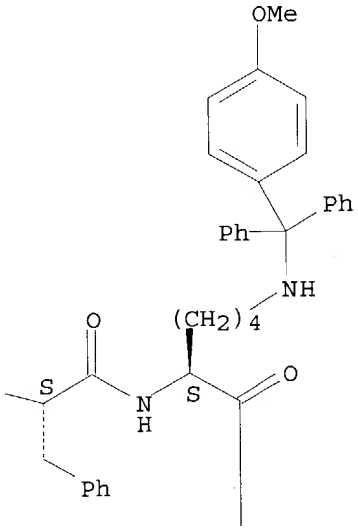
1,3-propanediyl]bis(oxycarbonyl)]bis[L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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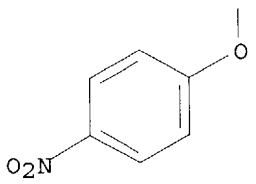

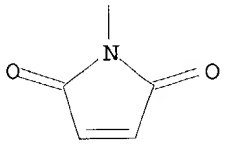

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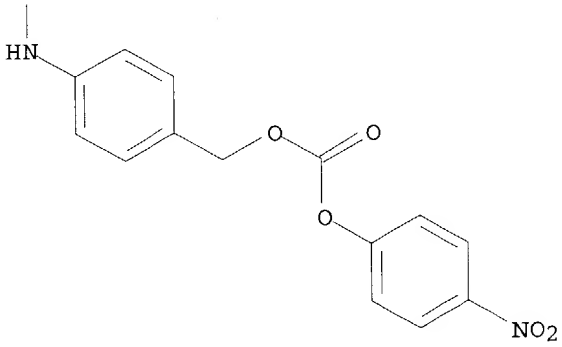


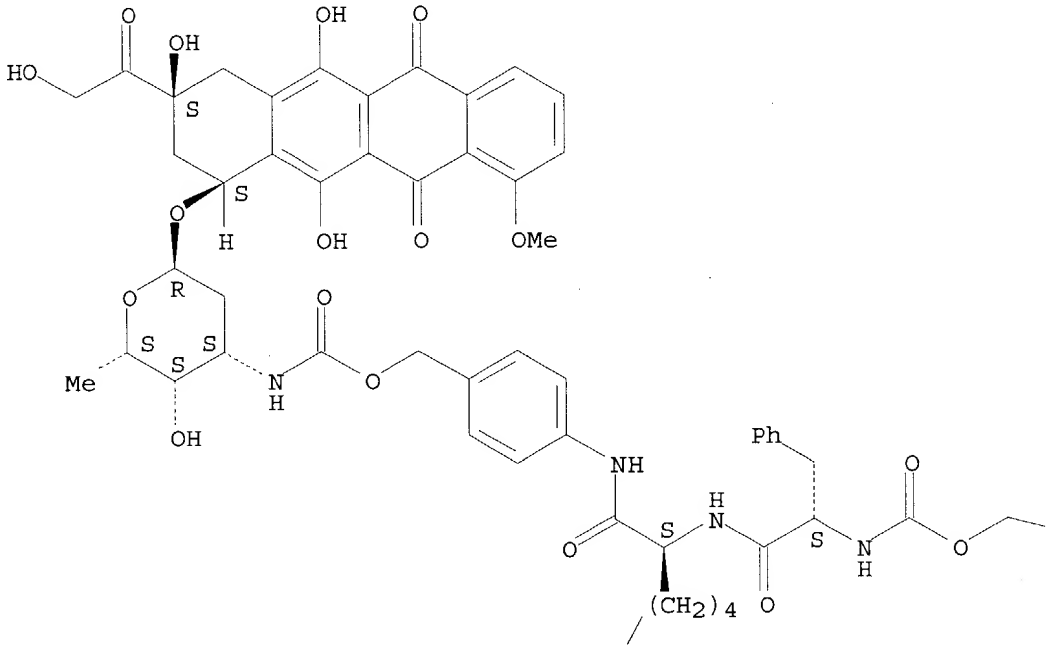
RN 207613-37-4 HCAPLUS
CN L-Lysinamide, 1,1'-[[2-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]-1,3-propanediyl]bis(oxycarbonyl)]bis[L-phenylalanyl-N-[4-

Searched by P. Ruppel

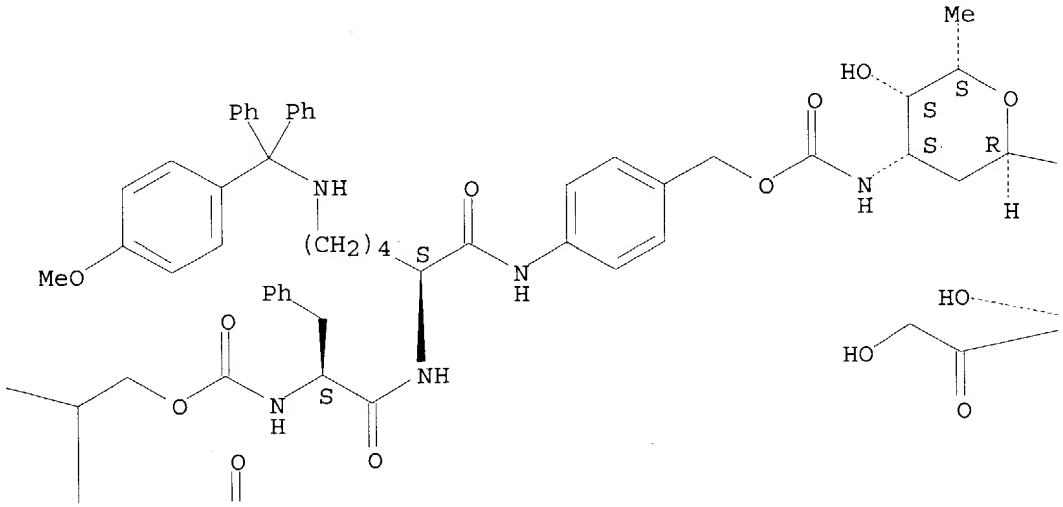
(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

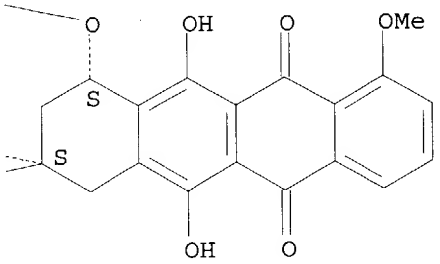
PAGE 1-A



PAGE 1-B

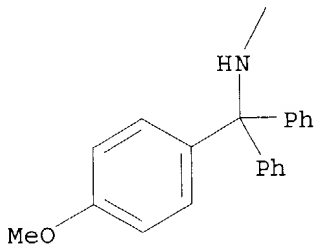


PAGE 1-C

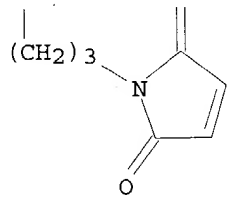


Searched by P. Ruppel

PAGE 2-A



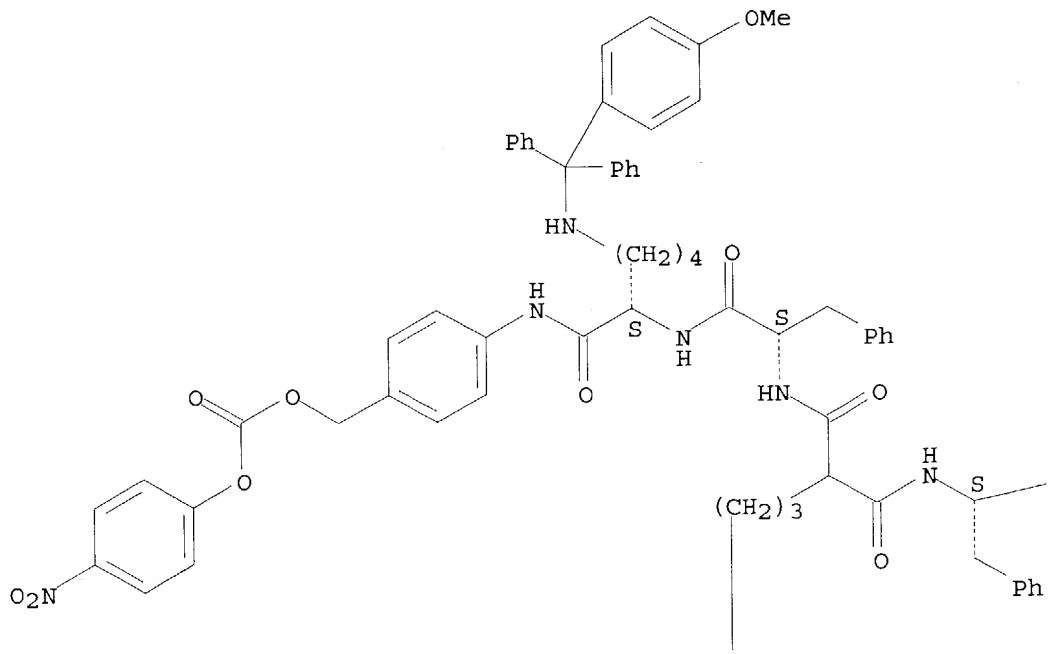
PAGE 2-B



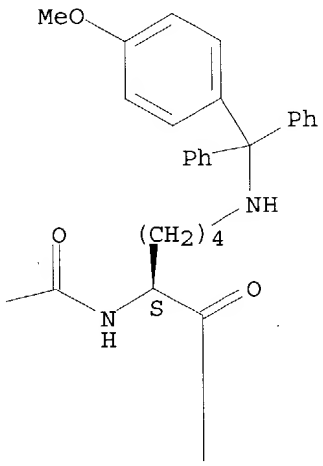
RN 207613-48-7 HCAPLUS
CN L-Lysinamide, 1,1'-[2-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]-1,3-dioxo-1,3-propanediyl]bis[L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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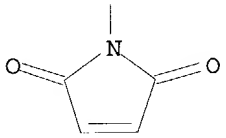
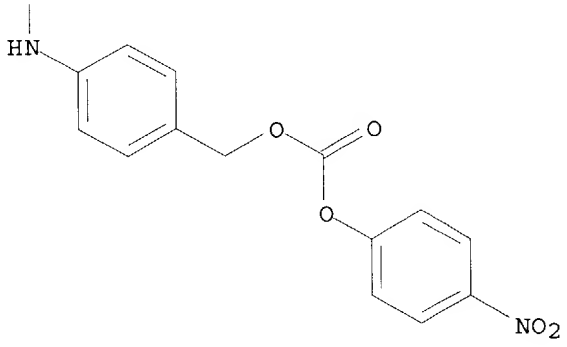


PAGE 2-B

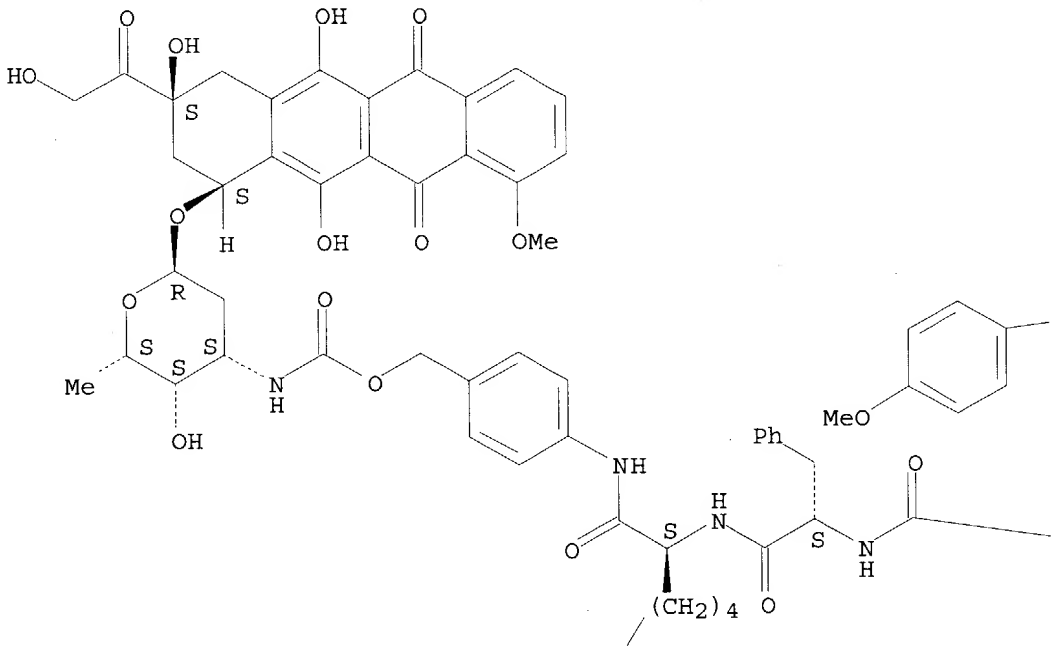


RN 207613-49-8 HCAPLUS
CN L-Lysinamide, 1,1'-[2-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]-1,3-dioxo-1,3-propanediyl]bis[L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, diester with (8S,10S)-10-[[3-

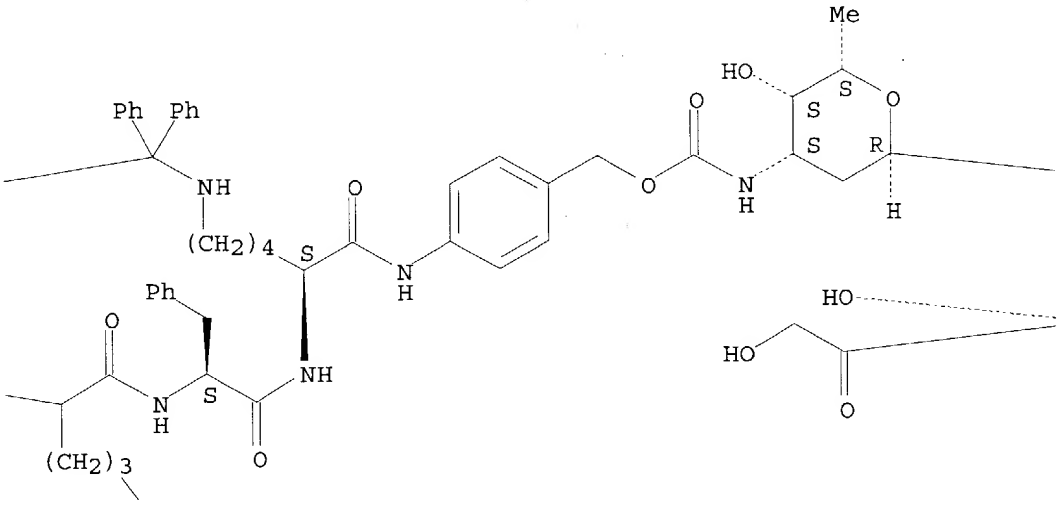
(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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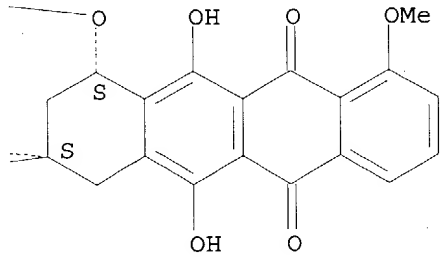
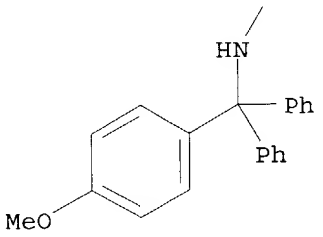
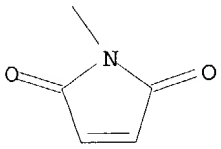


Searched by P. Ruppel

PAGE 2-A



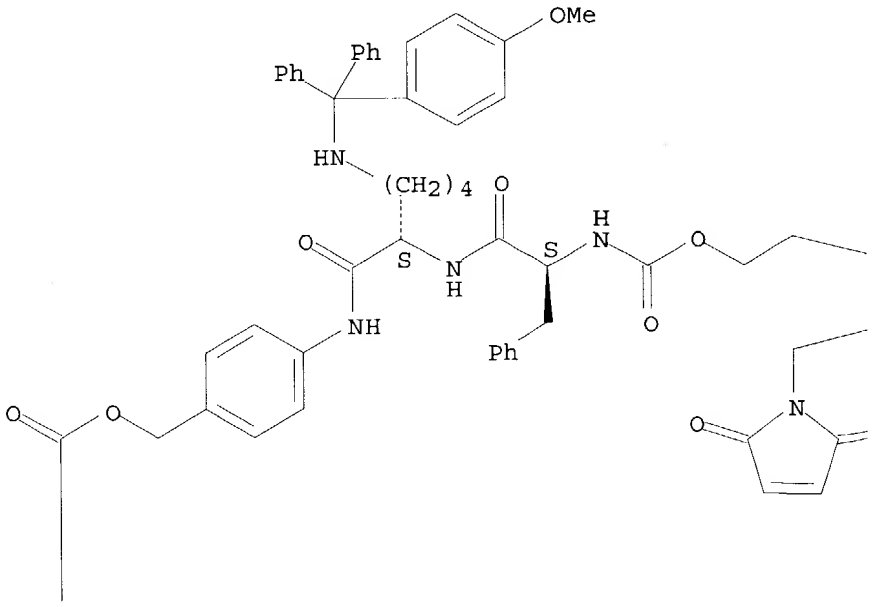
PAGE 2-B



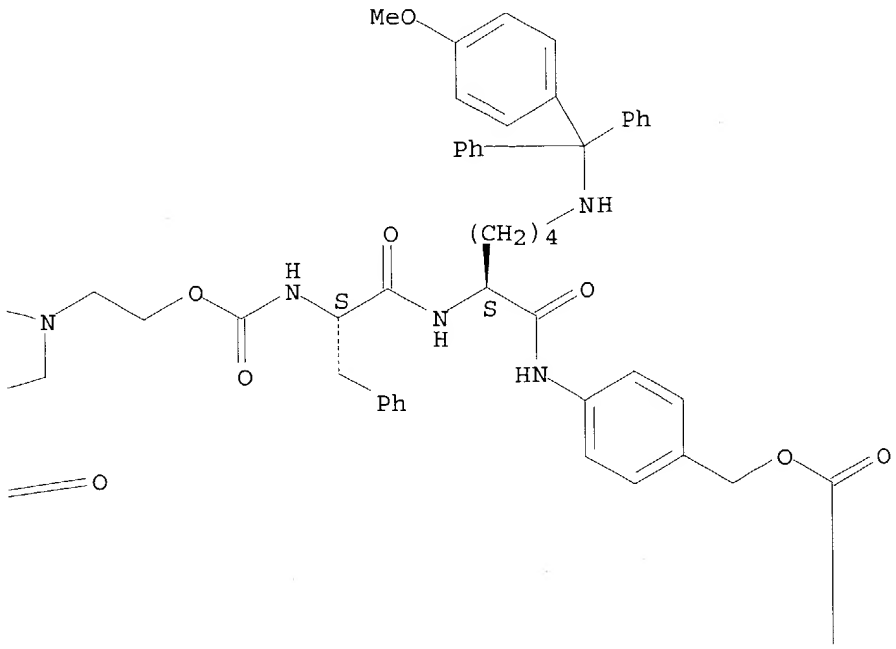
RN 207613-56-7 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(2,1-ethanediyloxycarbonyl)]bis[L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

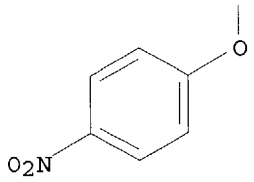
PAGE 1-A



PAGE 1-B



PAGE 2-A



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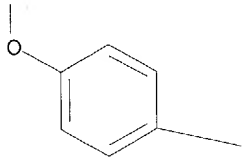

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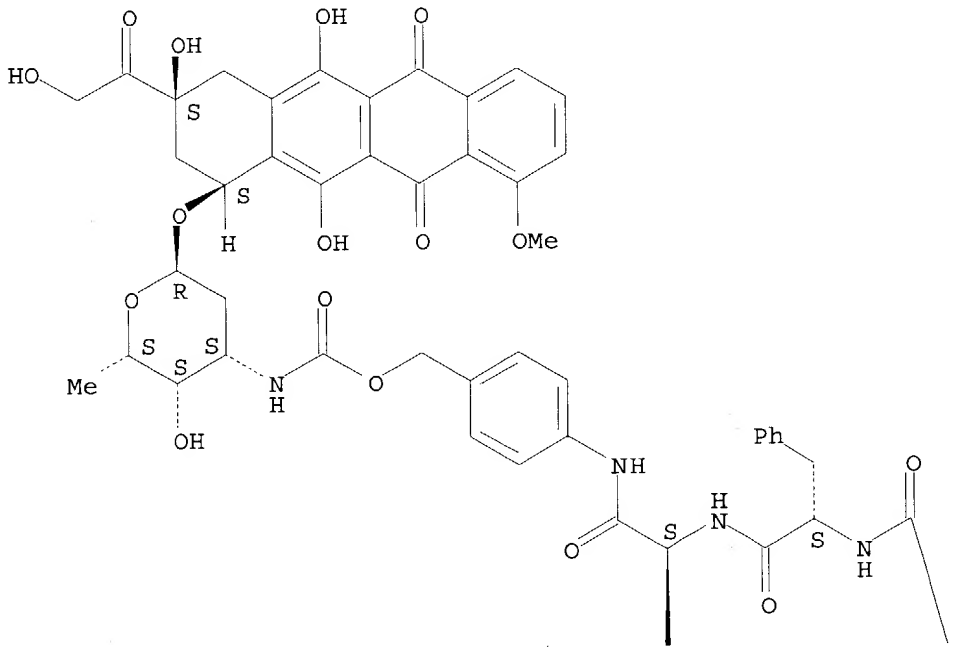
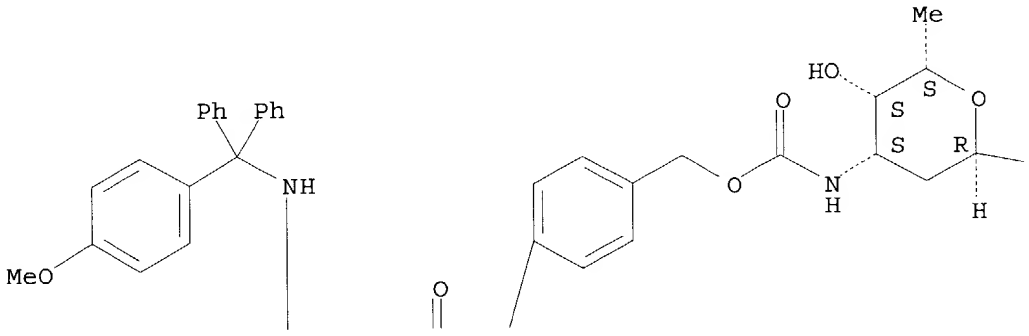
RN 207613-57-8 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(2,1-ethanediyloxycarbonyl)]bis[L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

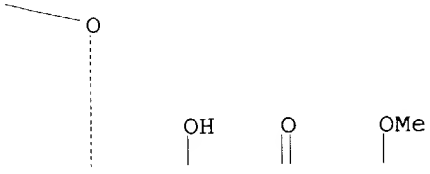
PAGE 1-A



PAGE 1-B

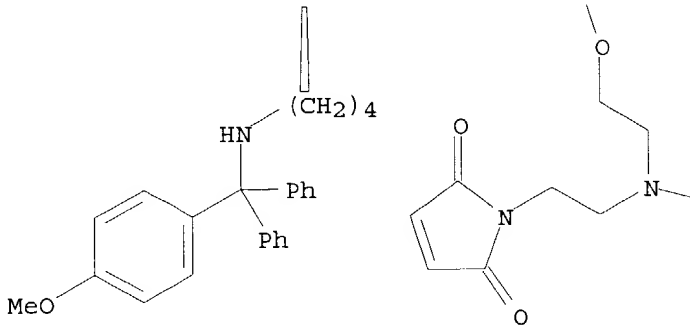


PAGE 1-C



Searched by P. Ruppel

PAGE 2-A



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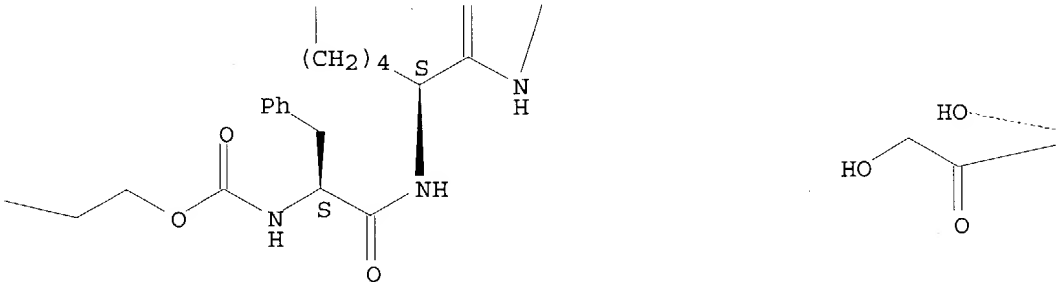

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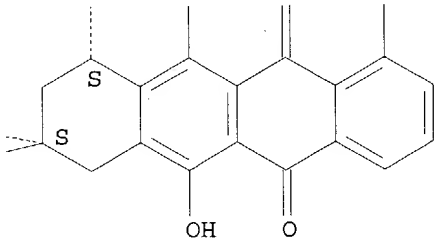
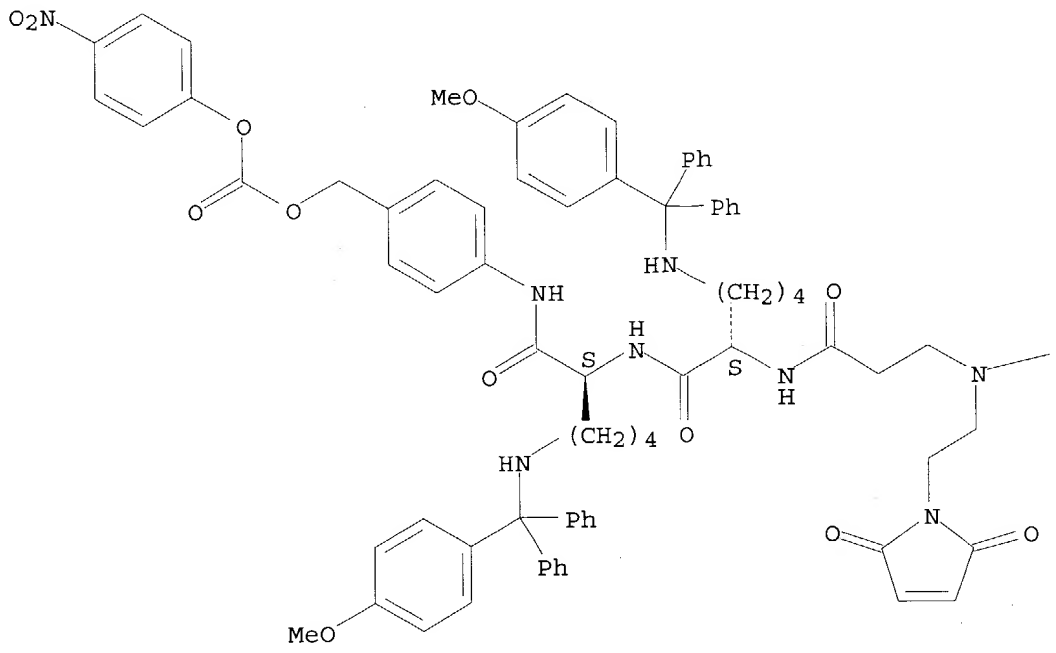


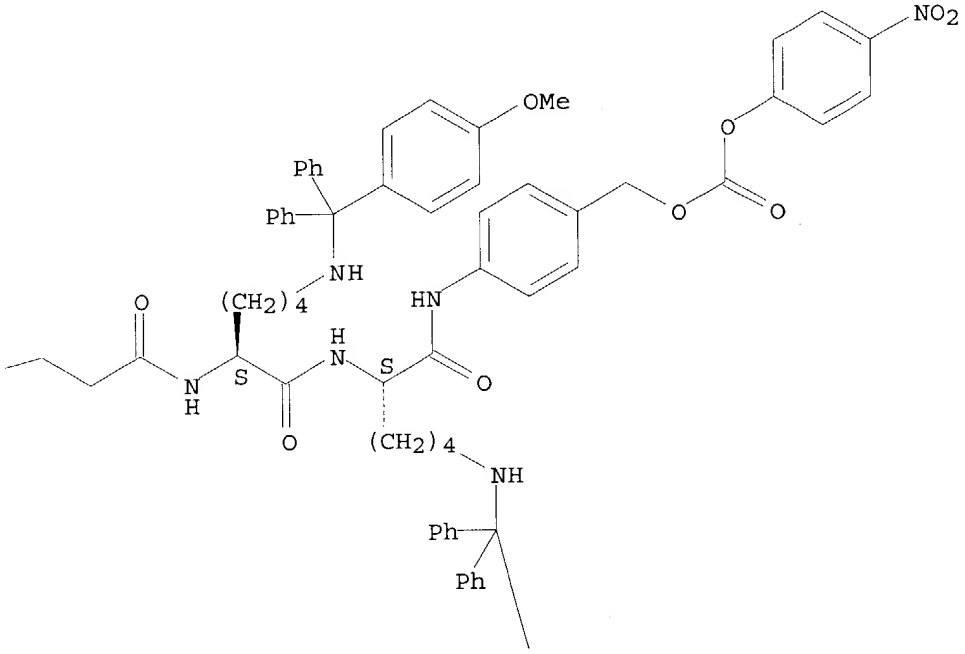
RN 207613-64-7 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

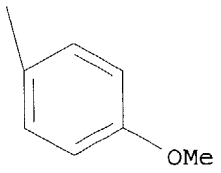


PAGE 1-B



Searched by P. Ruppel

PAGE 2-B



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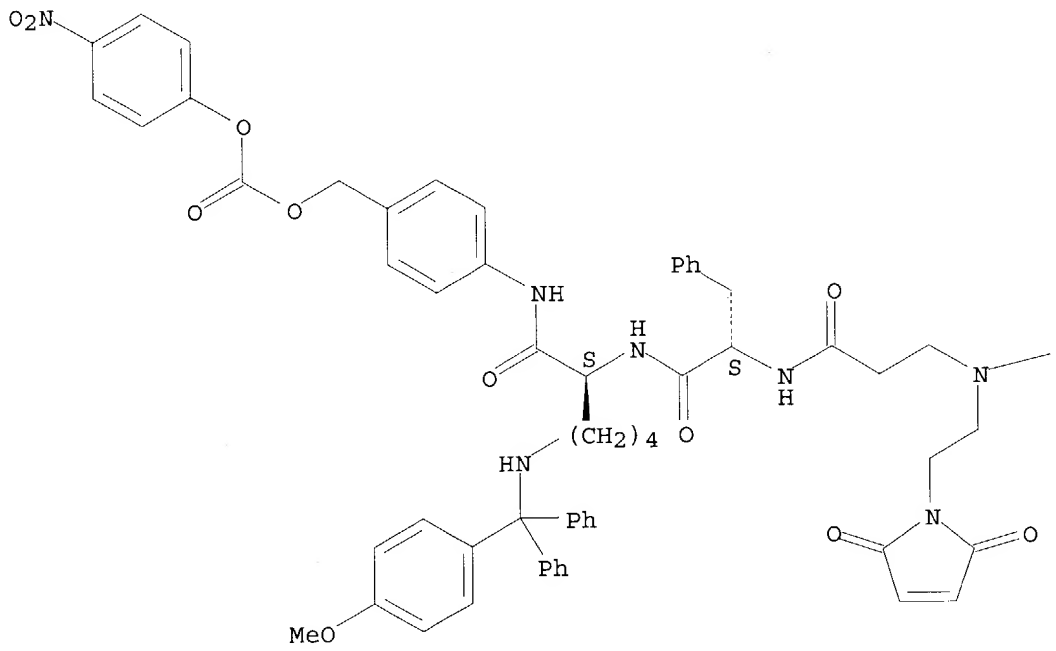
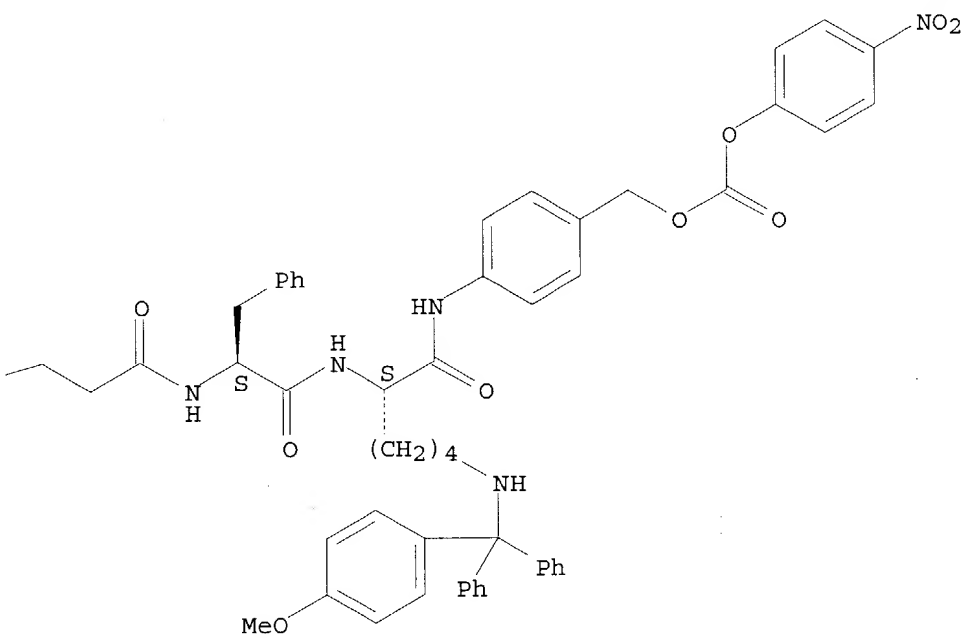
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



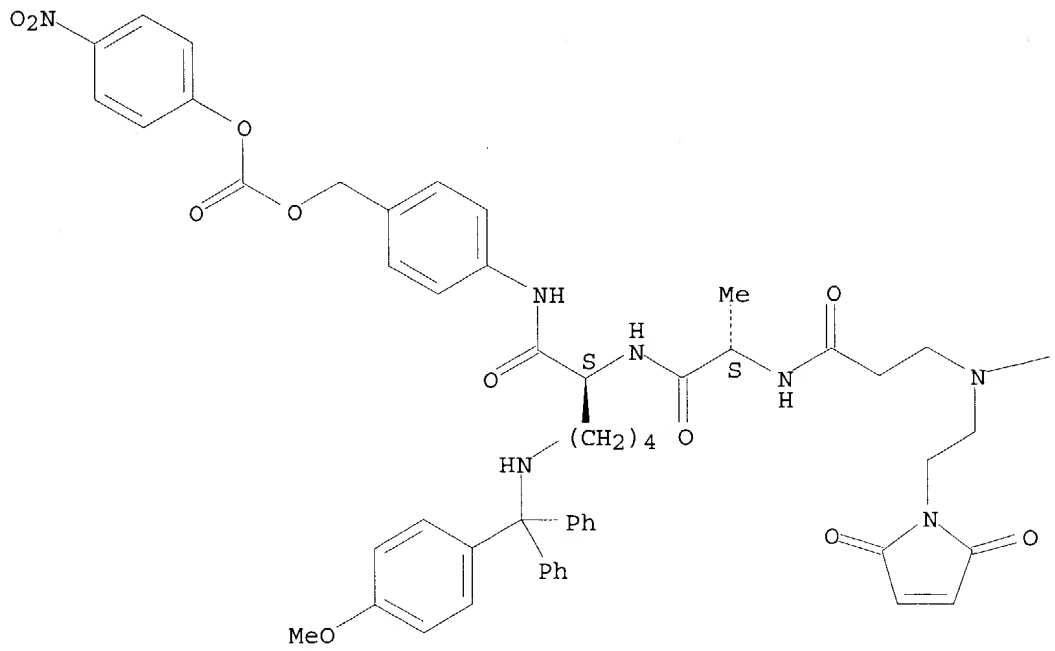
PAGE 1-B



RN 207613-66-9 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[L-alanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

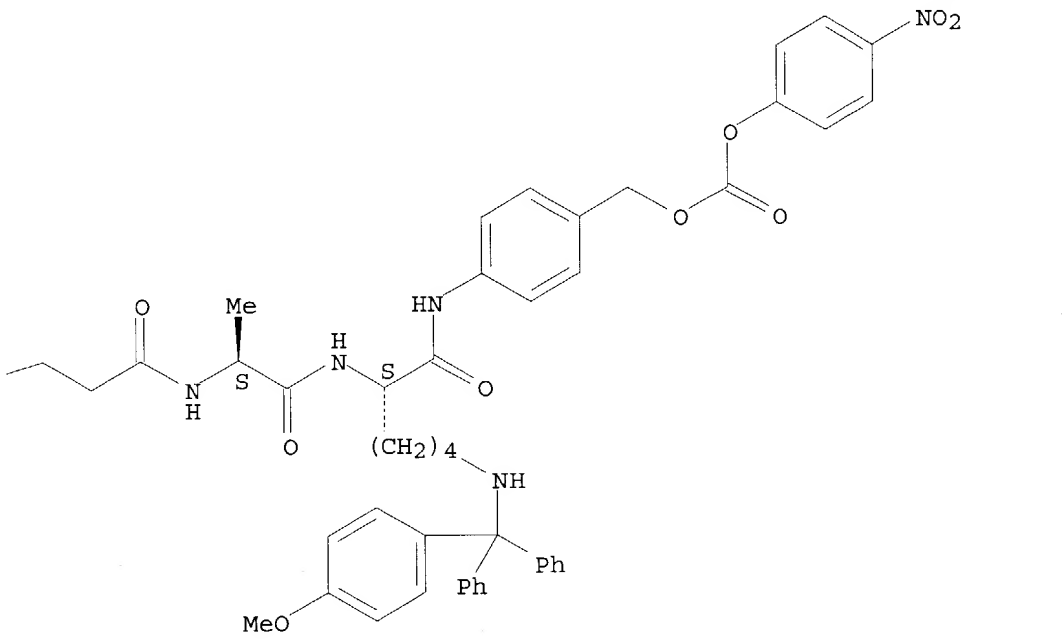
Absolute stereochemistry.

PAGE 1-A



Searched by P. Ruppel

PAGE 1-B

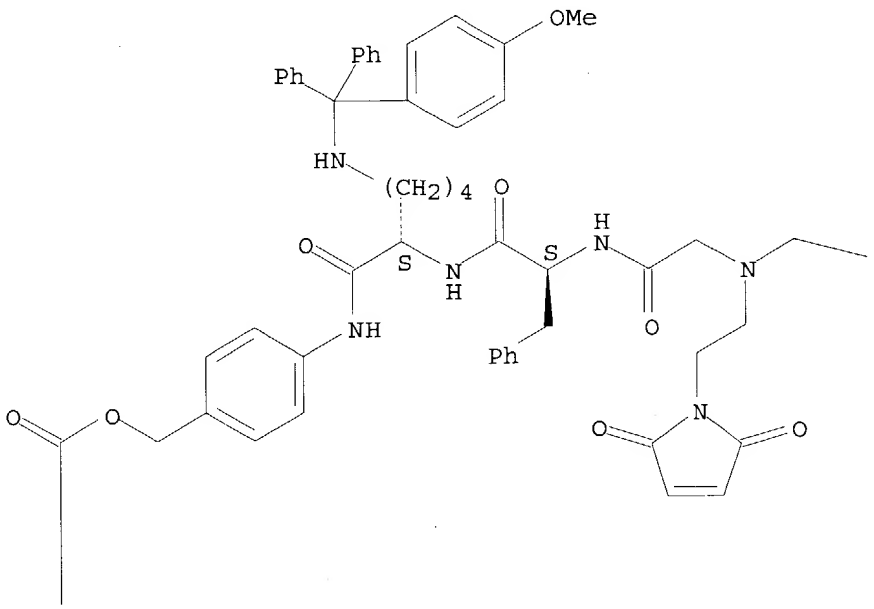


RN 207613-79-4 HCAPLUS

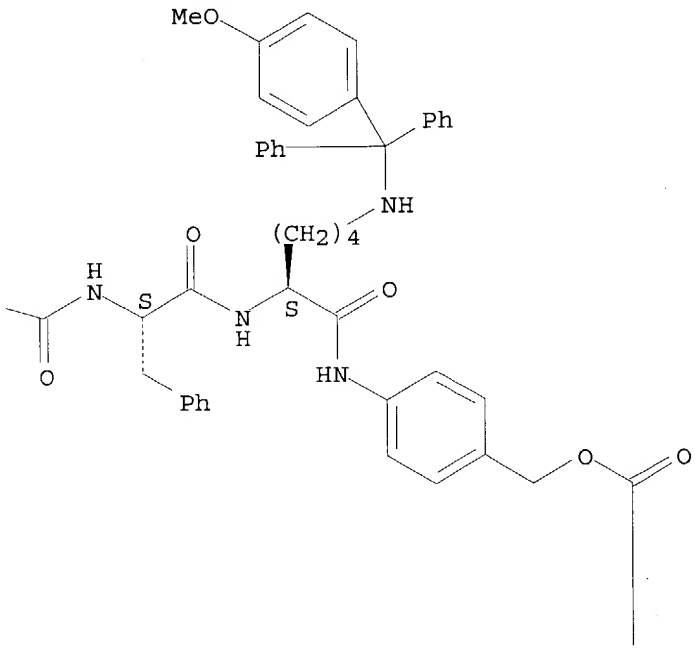
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-, (1→1')-amide with L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-L-lysinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

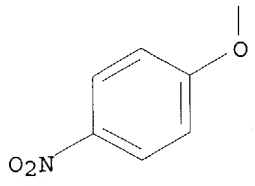


PAGE 1-B

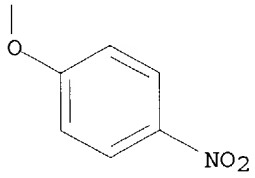


Searched by P. Ruppel

PAGE 2-A



PAGE 2-B

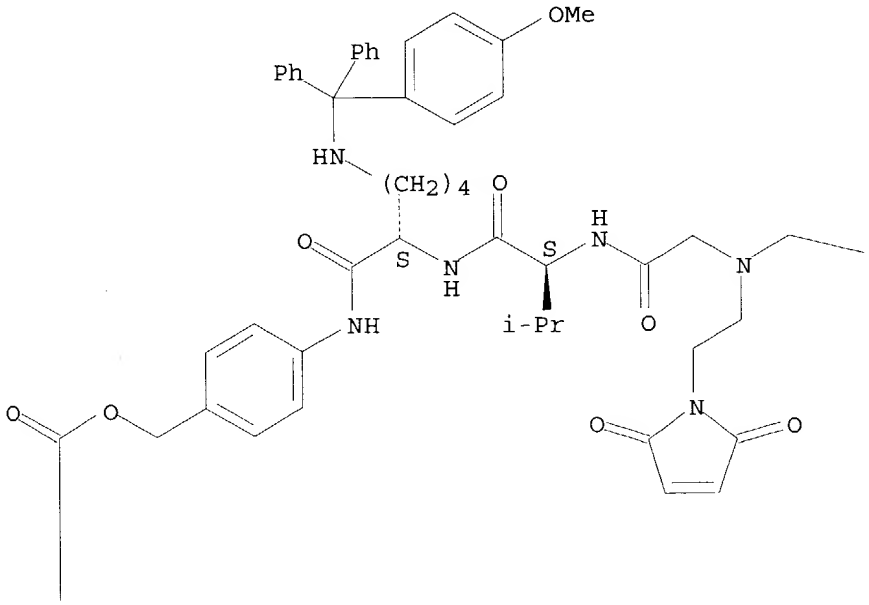


RN 207613-80-7 HCAPLUS

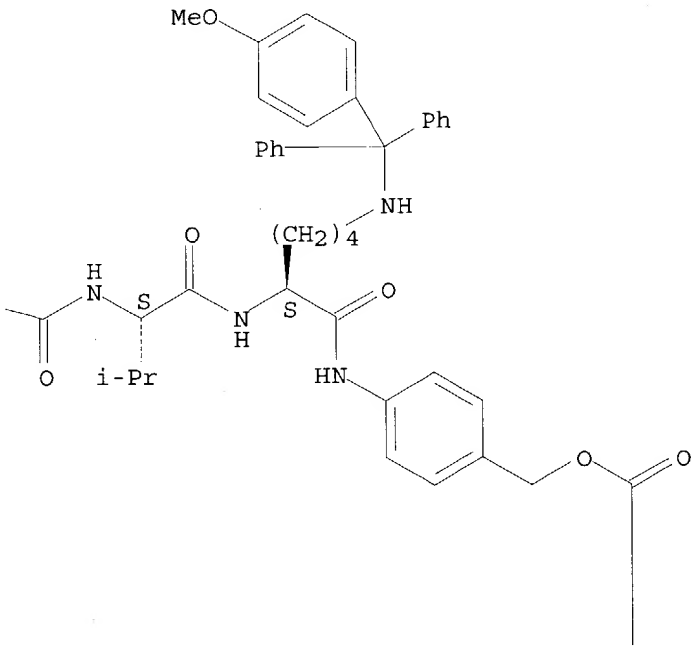
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-valyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-, (1→1')-amide with L-valyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-L-lysinamide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

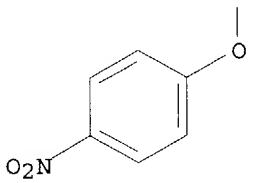
PAGE 1-A



PAGE 1-B



PAGE 2-A



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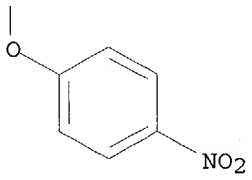


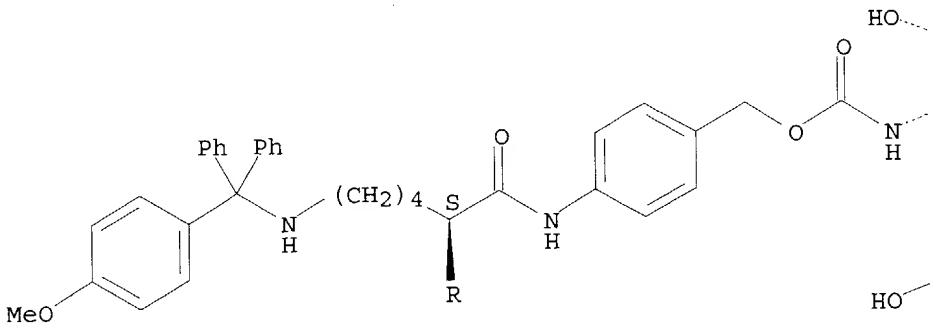
RN 207613-81-8 HCAPLUS

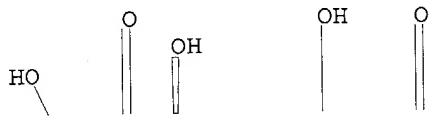
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Searched by P. Ruppel

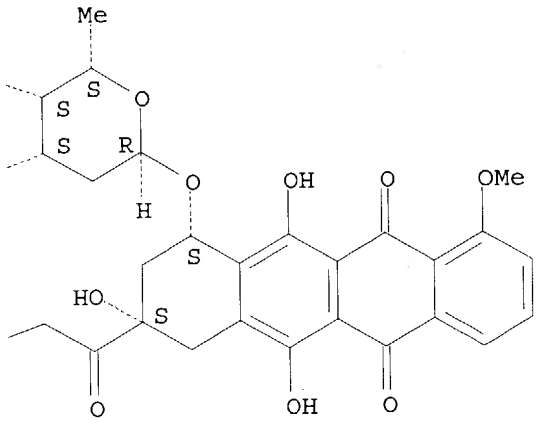
Absolute stereochemistry.

PAGE 1-A



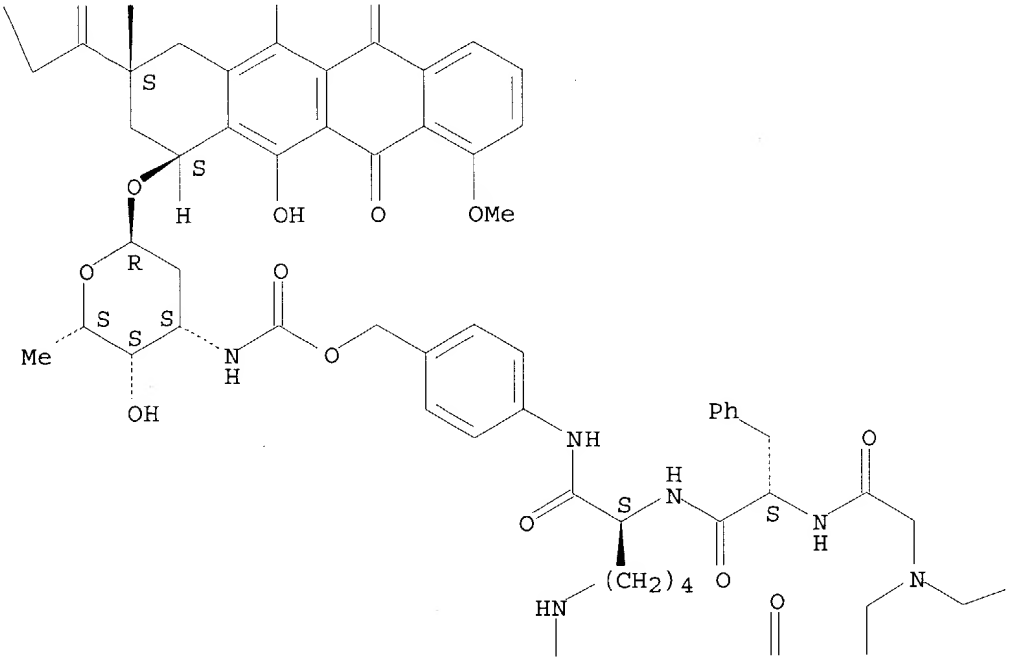


PAGE 1-B

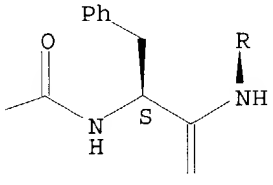


Searched by P. Ruppel

PAGE 2-A

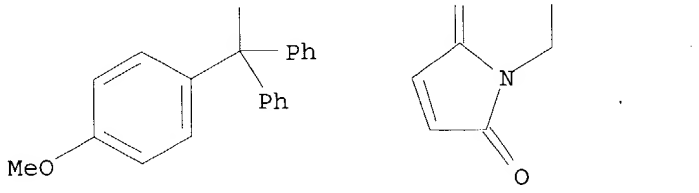


PAGE 2-B



Searched by P. Ruppel

PAGE 3-A

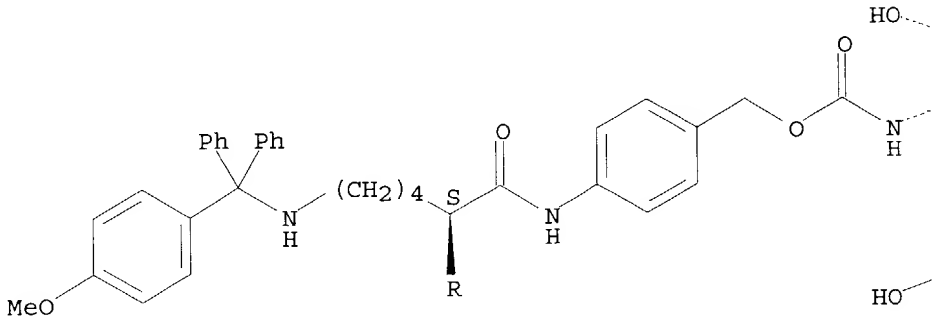


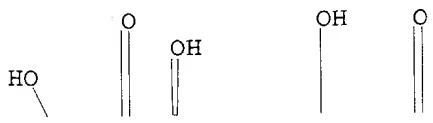
PAGE 3-B

RN 207613-82-9 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-valyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-valyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

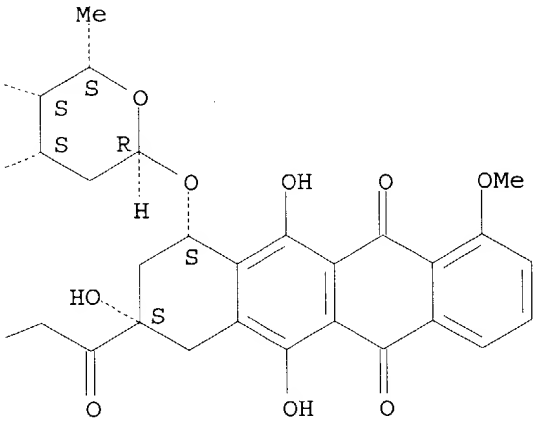
Absolute stereochemistry.

PAGE 1-A

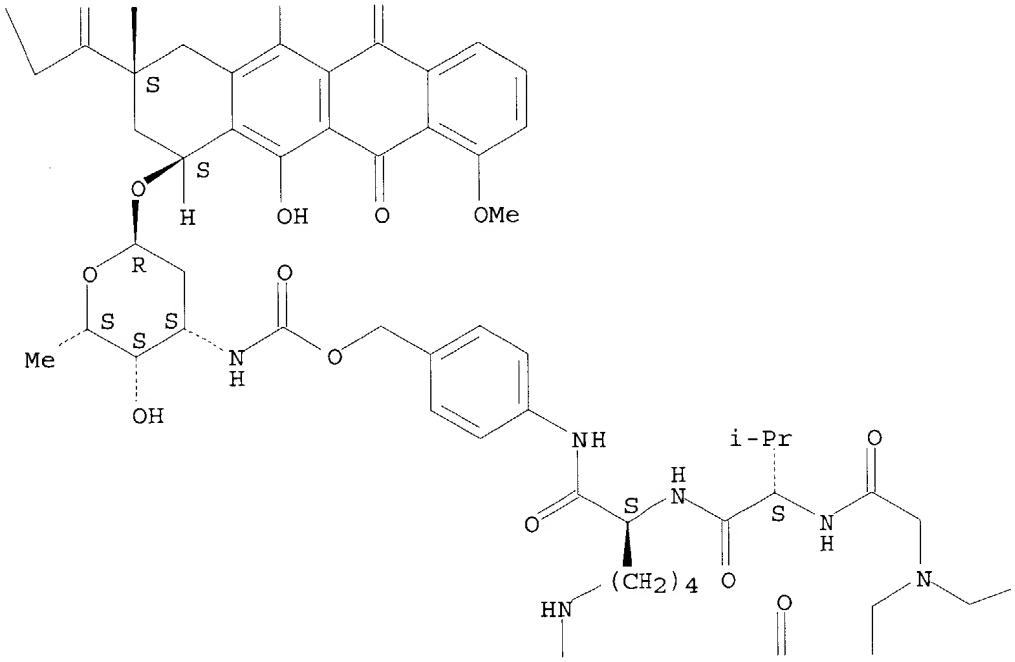




PAGE 1-B



PAGE 2-A



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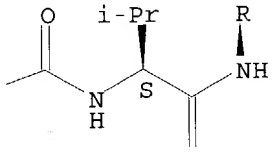
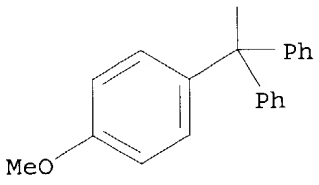
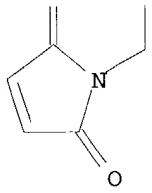


PAGE 3-A





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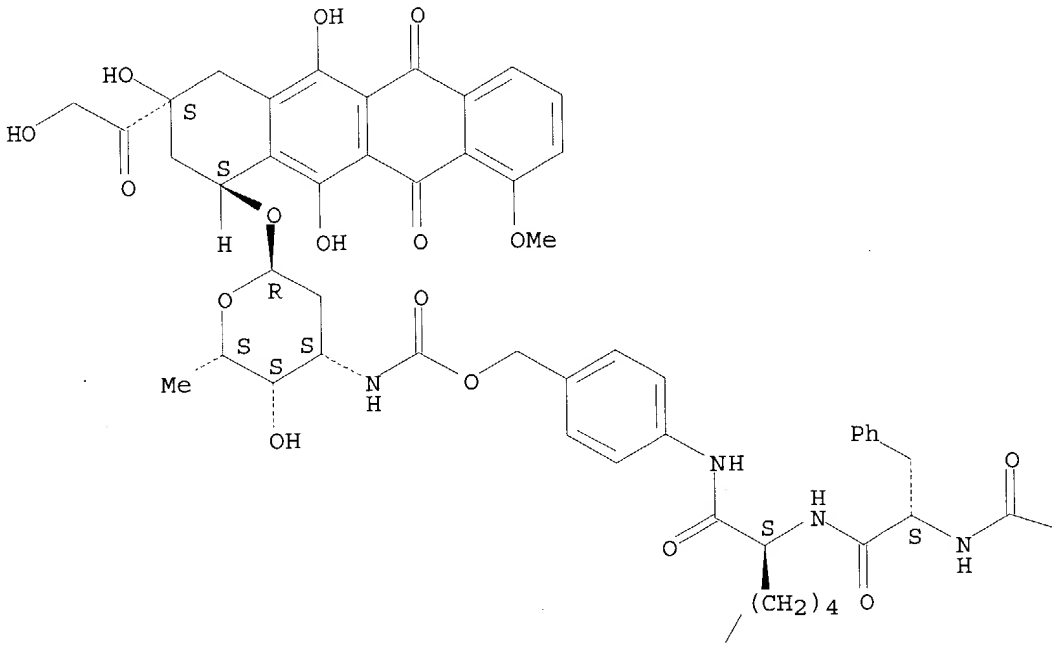
RN 207613-83-0 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

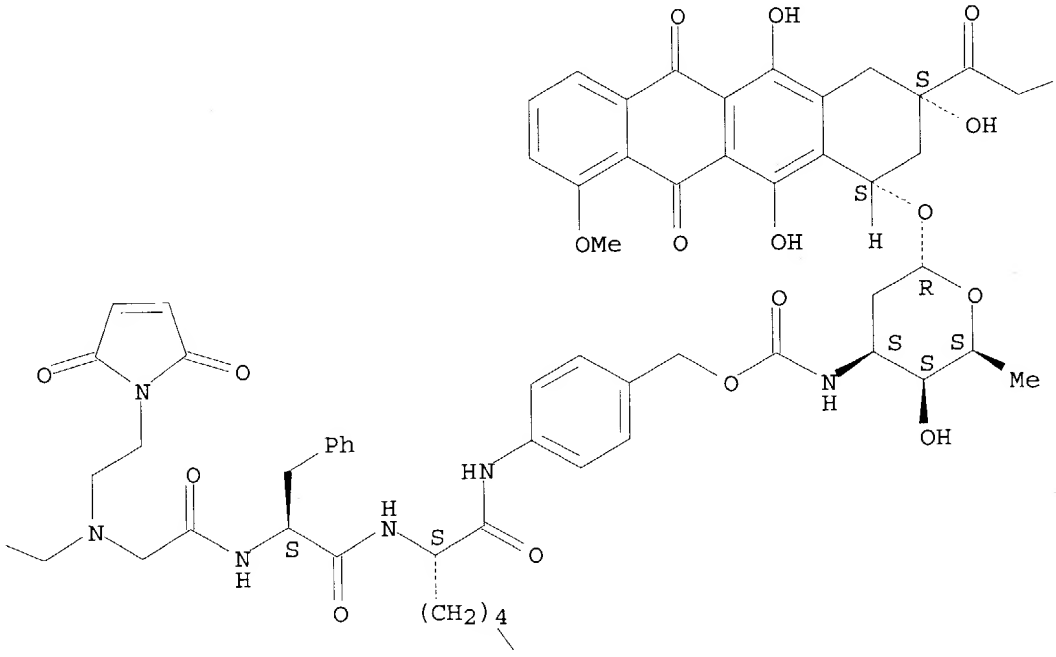
Absolute stereochemistry.

Searched by P. Ruppel

PAGE 1-A



PAGE 1-B



Searched by P. Ruppel

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IT **207612-99-5P 207613-01-2P 207613-12-5P**
207613-19-2P 207613-32-9P 207613-39-6P
207613-51-2P 207613-59-0P 207613-67-0P
207613-68-1P 207613-69-2P 207613-71-6P
207613-73-8P 207613-75-0P 207613-84-1P
207613-86-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of branched peptide linkers)

RN 207612-99-5 HCAPLUS

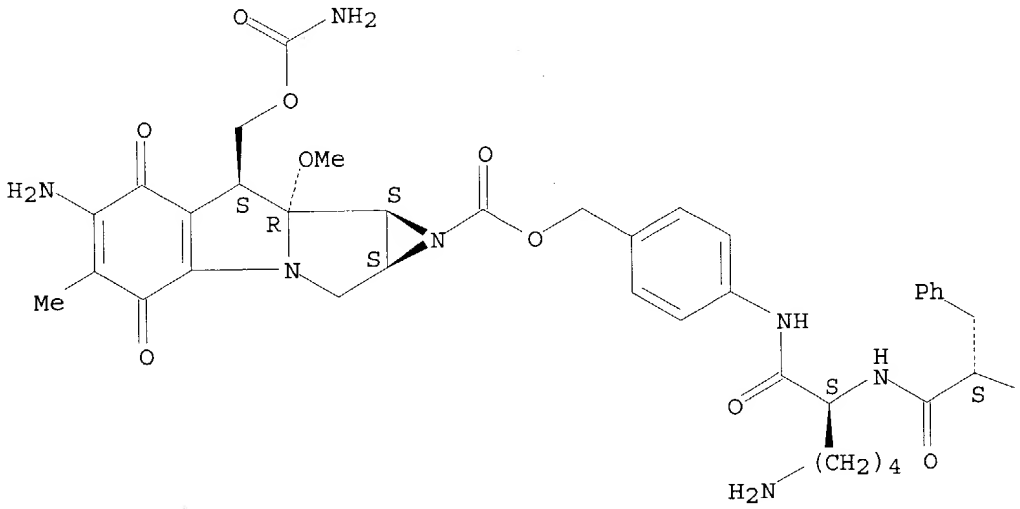
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N-[4-[[[[(1aS,8S,8aR,8bS)-6-amino-8-[[(aminocarbonyl)oxy]methyl]-1a,4,7,8,8a,8b-hexahydro-8a-methoxy-5-methyl-4,7-dioxoazirino[2',3':3,4]pyrrolo[1,2-a]indol-1(2H)-yl]carbonyl]oxy]methyl]phenyl]-, (1→1')-amide with L-phenylalanyl-N-[4-[[[[(1aS,8S,8aR,8bS)-6-amino-8-[[(aminocarbonyl)oxy]methyl]-1a,4,7,8,8a,8b-hexahydro-8a-methoxy-5-methyl-4,7-dioxoazirino[2',3':3,4]pyrrolo[1,2-a]indol-1(2H)-yl]carbonyl]oxy]methyl]phenyl]-L-lysinamide, bis(chloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

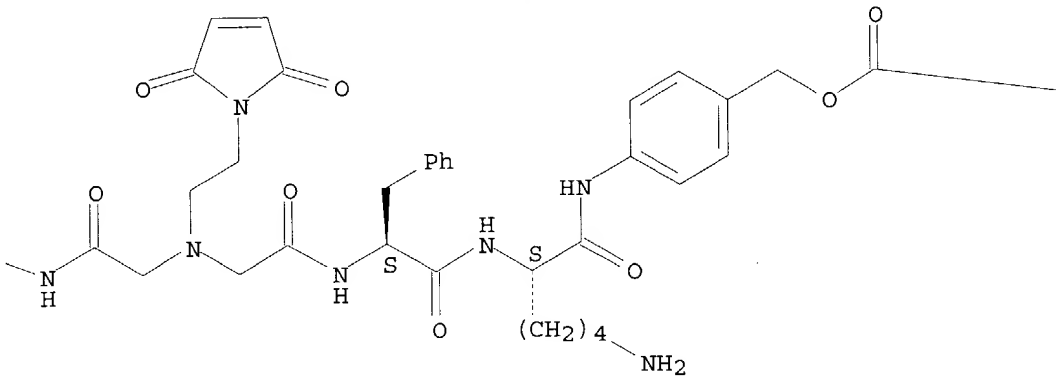
CRN 207612-98-4
CMF C86 H100 N18 O22

Absolute stereochemistry.

PAGE 1-A

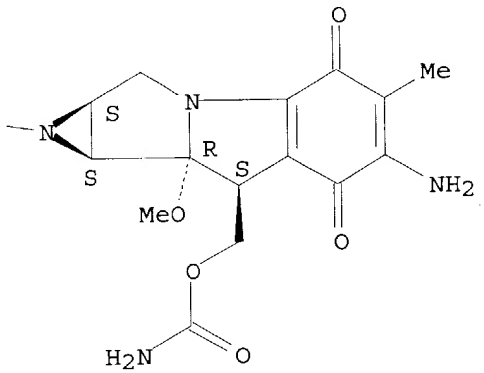


PAGE 1-B



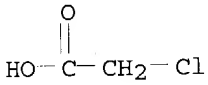
Searched by P. Ruppel

PAGE 1-C



CM 2

CRN 79-11-8
CMF C2 H3 Cl O2



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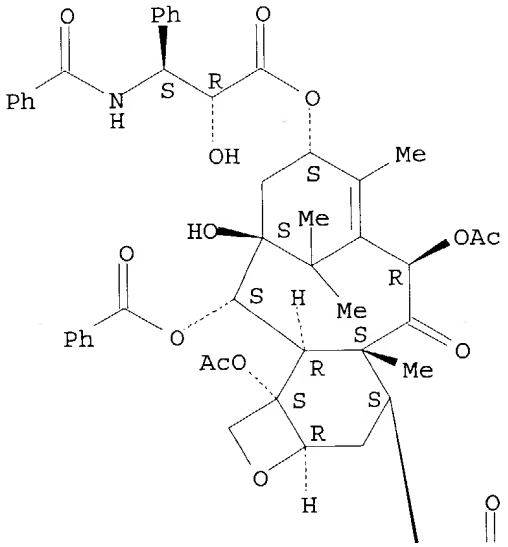
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N-[4-[[[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]oxy]methyl]phenyl]-, (1→1')-amide with L-phenylalanyl-N-[4-[[[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]oxy]methyl]phenyl]-L-lysinamide, bis(chloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 207613-00-1
CMF C150 H166 N12 O40

Absolute stereochemistry.

PAGE 1-A



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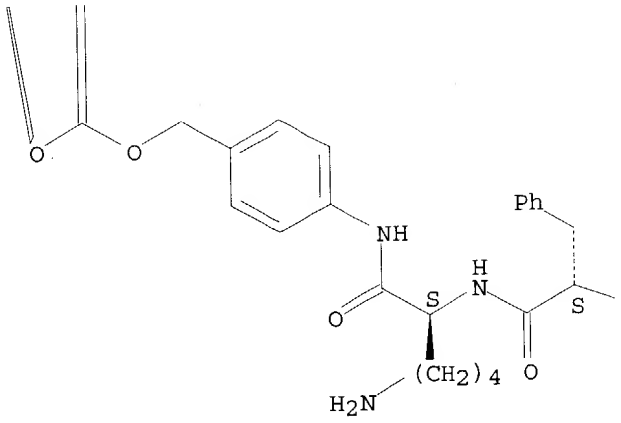
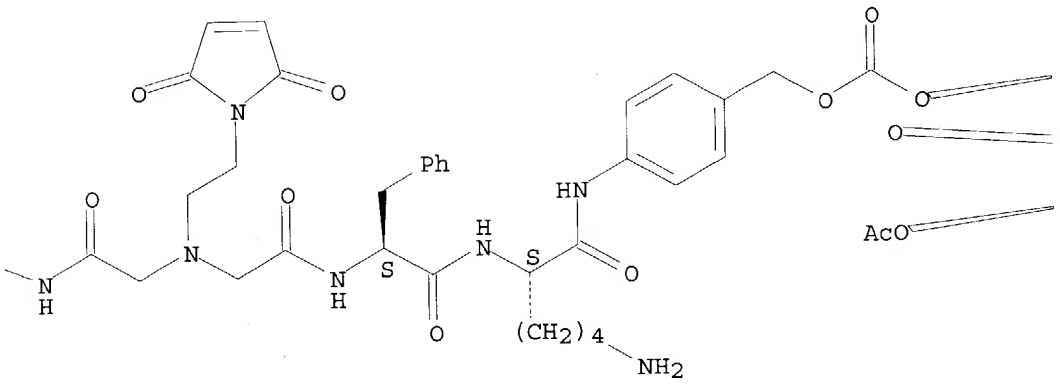
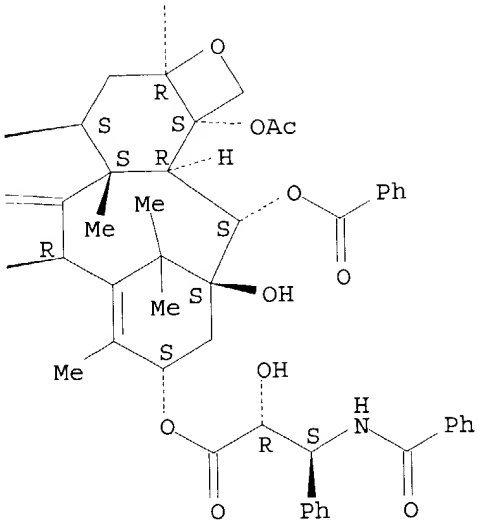


PAGE 2-B

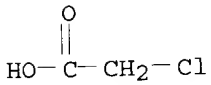


PAGE 2-C



CM 2

CRN 79-11-8
CMF C2 H3 Cl O2



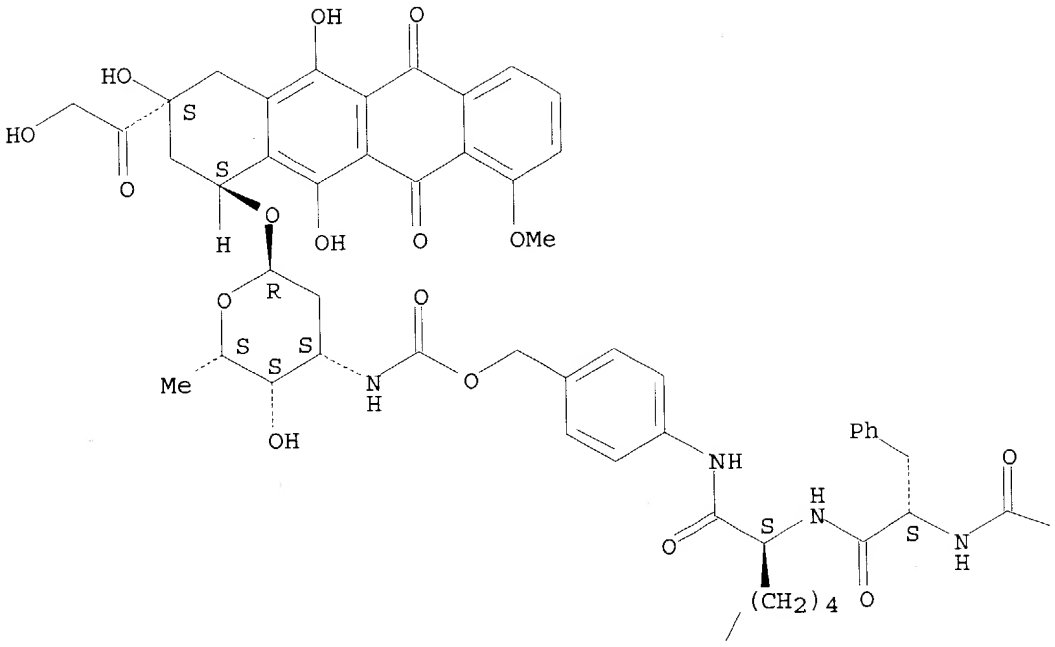
RN 207613-12-5 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, bis(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

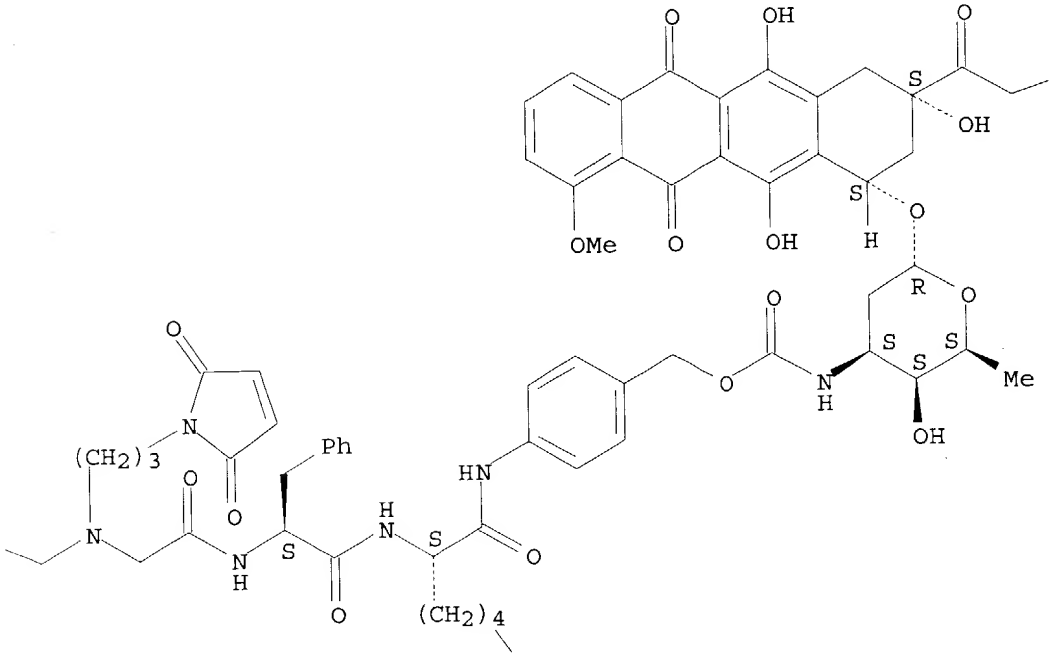
CRN 207613-11-4
CMF C111 H124 N12 O34

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



Searched by P. Ruppel

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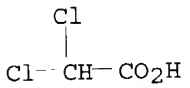
CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2



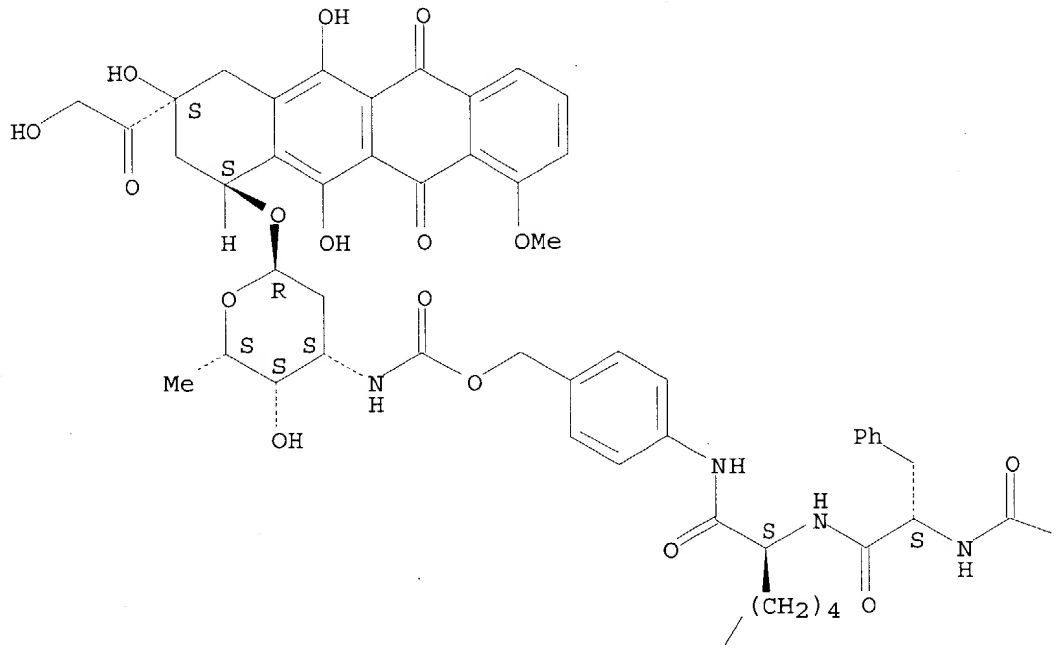
RN 207613-19-2 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, bis(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 207613-18-1
CMF C111 H122 N12 O35

Absolute stereochemistry.

PAGE 1-A



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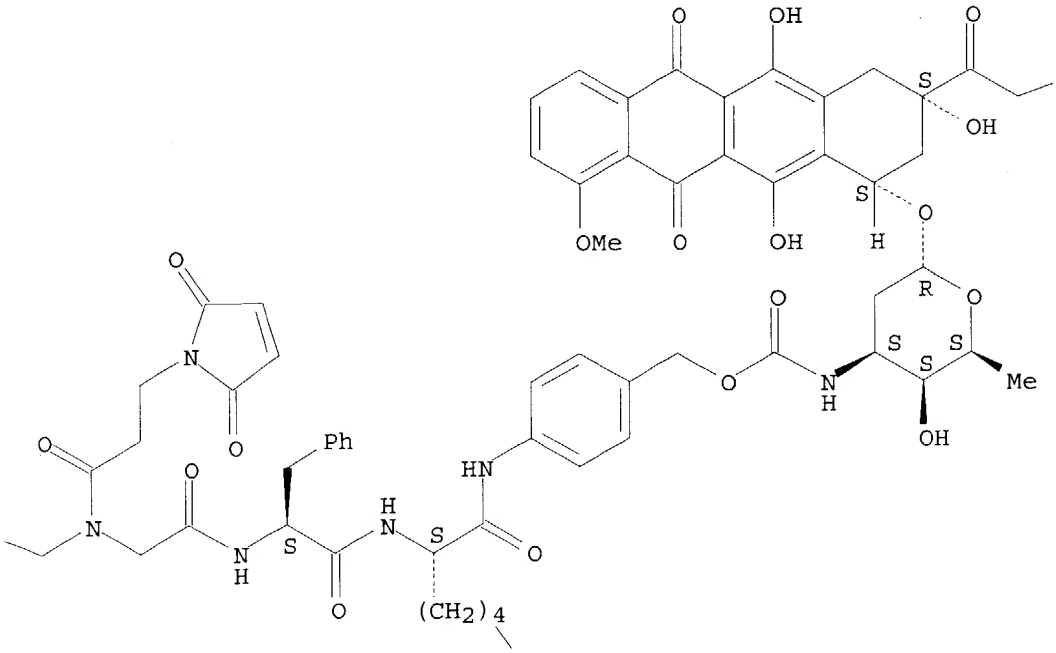

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PAGE 2-A

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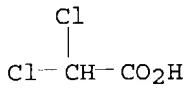
CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2



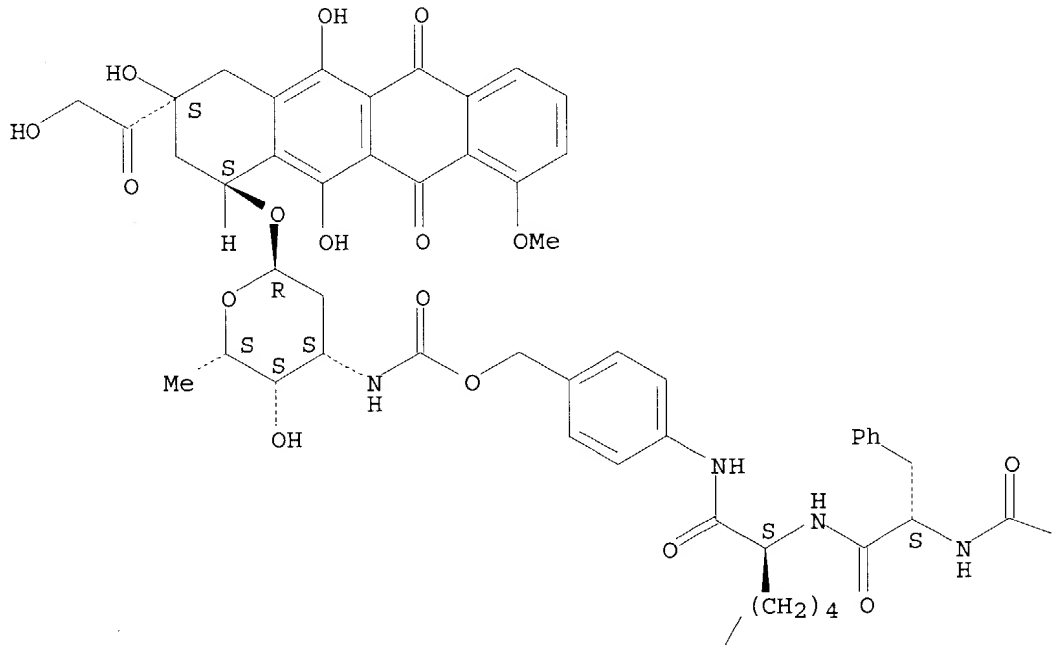
RN 207613-32-9 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]glycyl-β-alanyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, 4-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with β-alanyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, bis(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

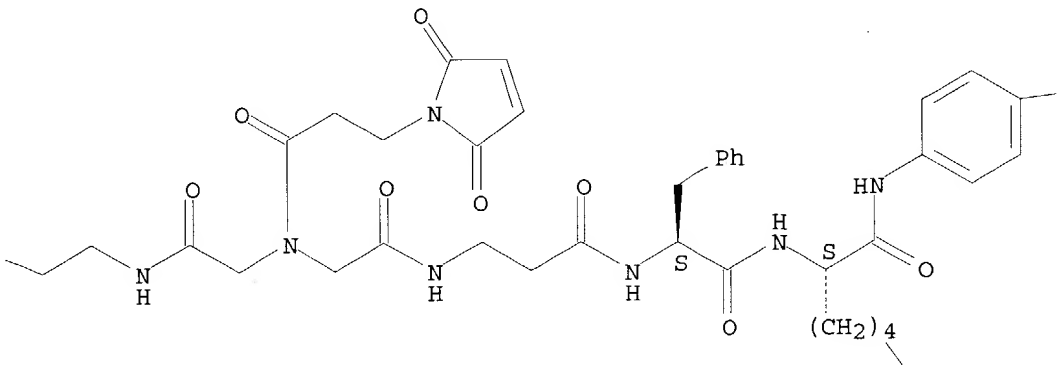
CRN 207613-31-8
CMF C117 H132 N14 O37

Absolute stereochemistry.

PAGE 1-A

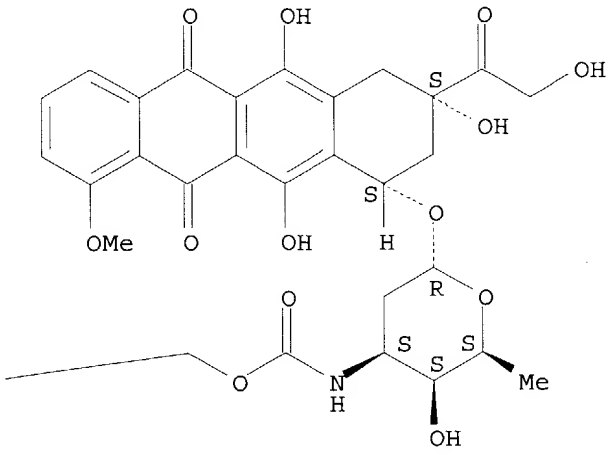


PAGE 1-B



Searched by P. Ruppel

PAGE 1-C



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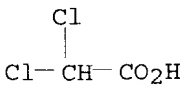
CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2



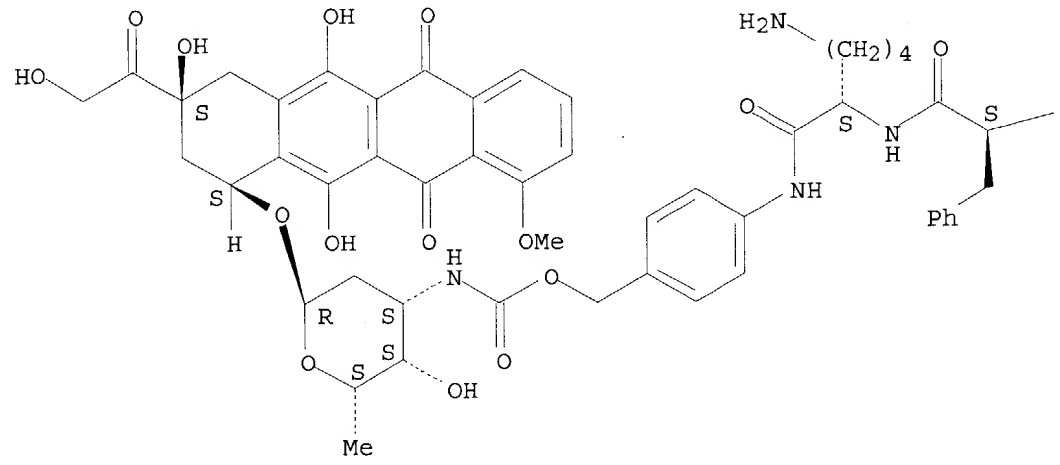
RN 207613-39-6 HCAPLUS
CN L-Lysinamide, 1,1'-[[2-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]-1,3-propanediyl]bis(oxycarbonyl)]bis[L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, bis(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 207613-38-5
CMF C112 H125 N11 O36

Absolute stereochemistry.

PAGE 1-A



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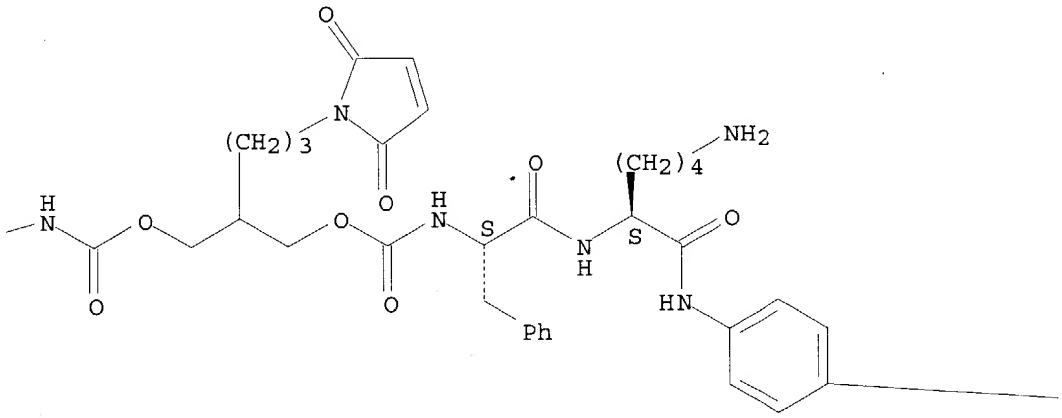
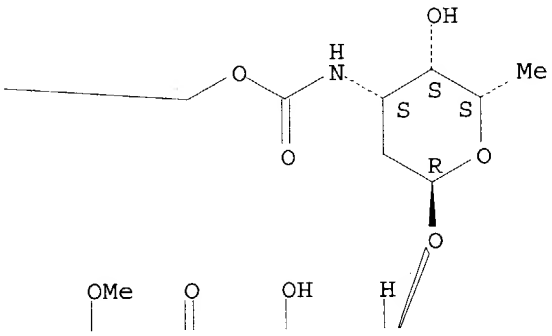


PAGE 1-C



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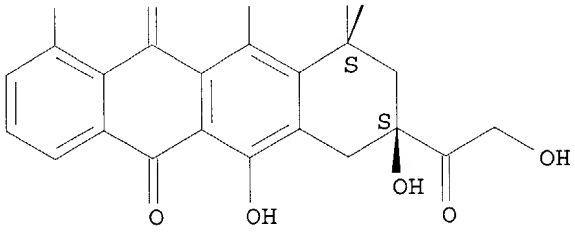
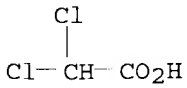


CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2



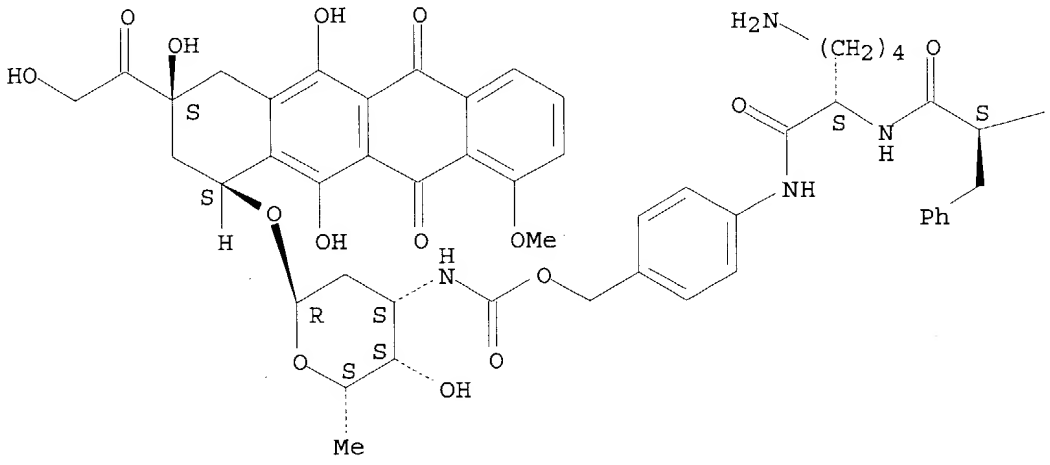
RN 207613-51-2 HCAPLUS
CN L-Lysinamide, 1,1'-[2-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propyl]-1,3-dioxo-1,3-propanediyl]bis[L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, bis(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

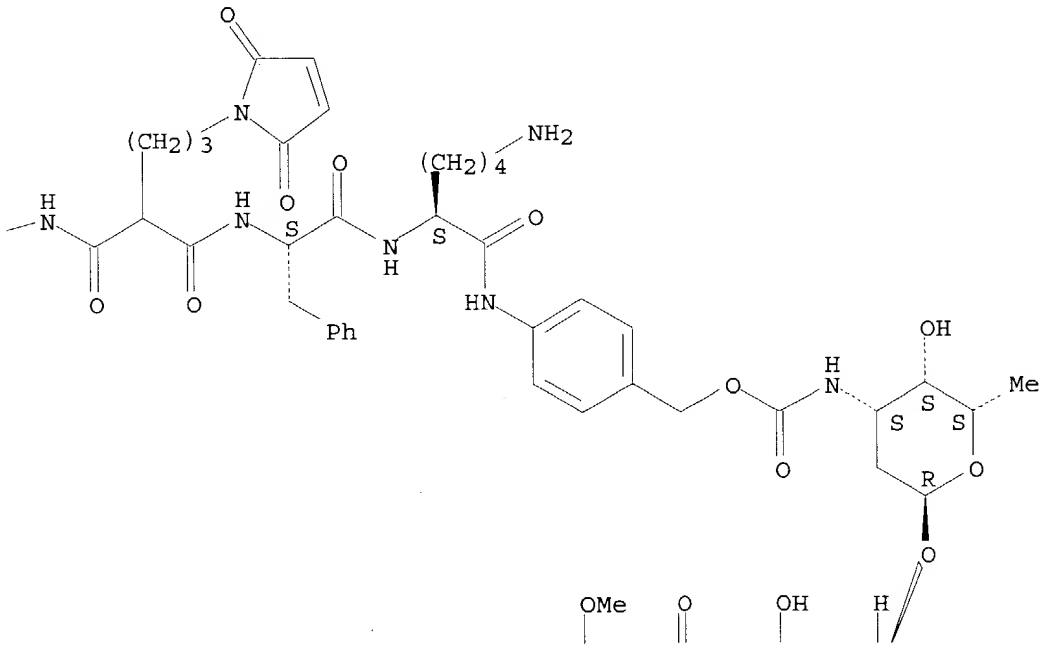
CRN 207613-50-1
CMF C110 H121 N11 O34

Absolute stereochemistry.

PAGE 1-A

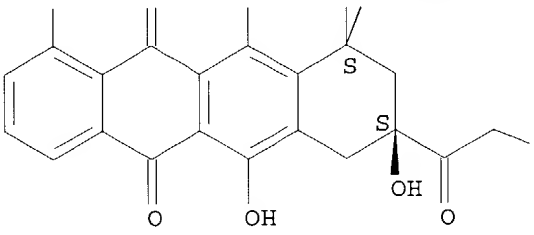


PAGE 1-B



Searched by P. Ruppel

PAGE 2-B



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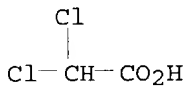
OH

CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2



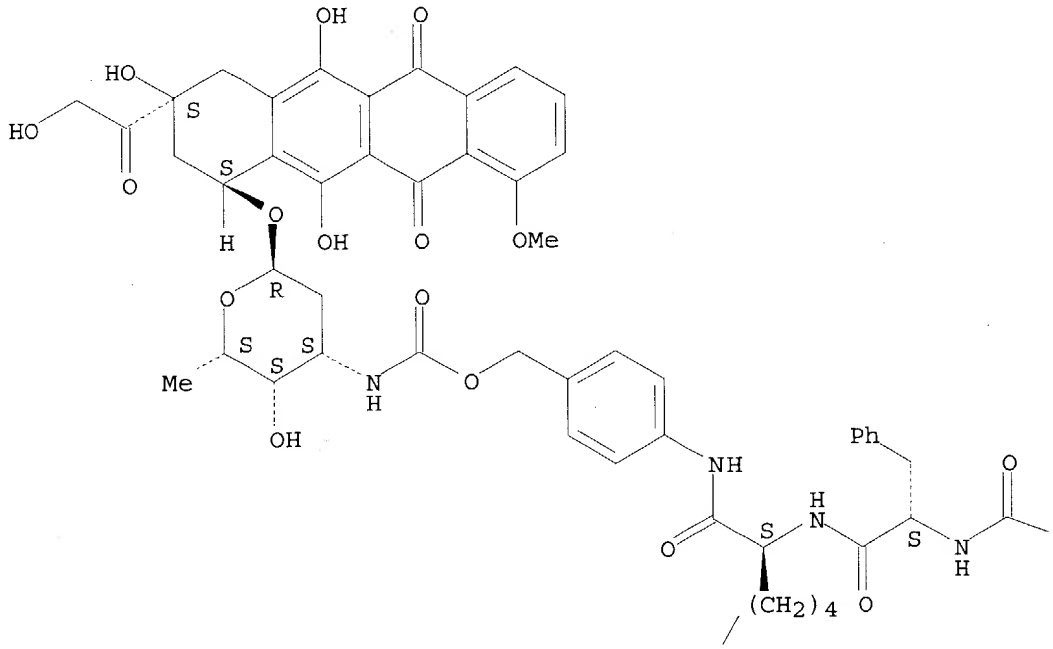
RN 207613-59-0 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(2,1-ethanediyloxycarbonyl)]bis[L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, bis(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 207613-58-9
CMF C112 H126 N12 O36

Absolute stereochemistry.

PAGE 1-A



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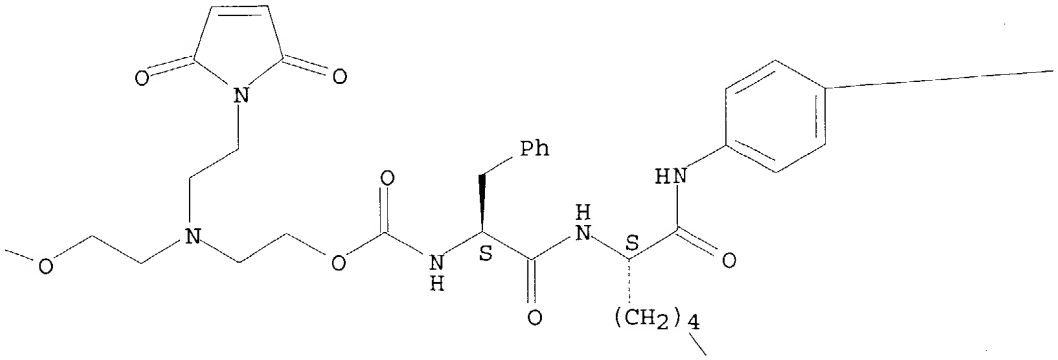
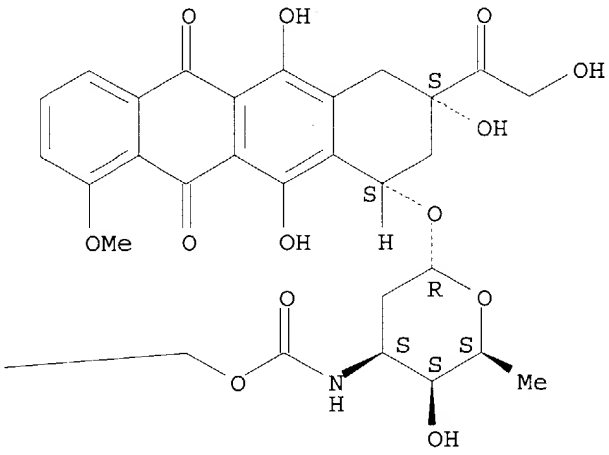


Searched by P. Ruppel

PAGE 1-C



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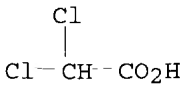
CM 2

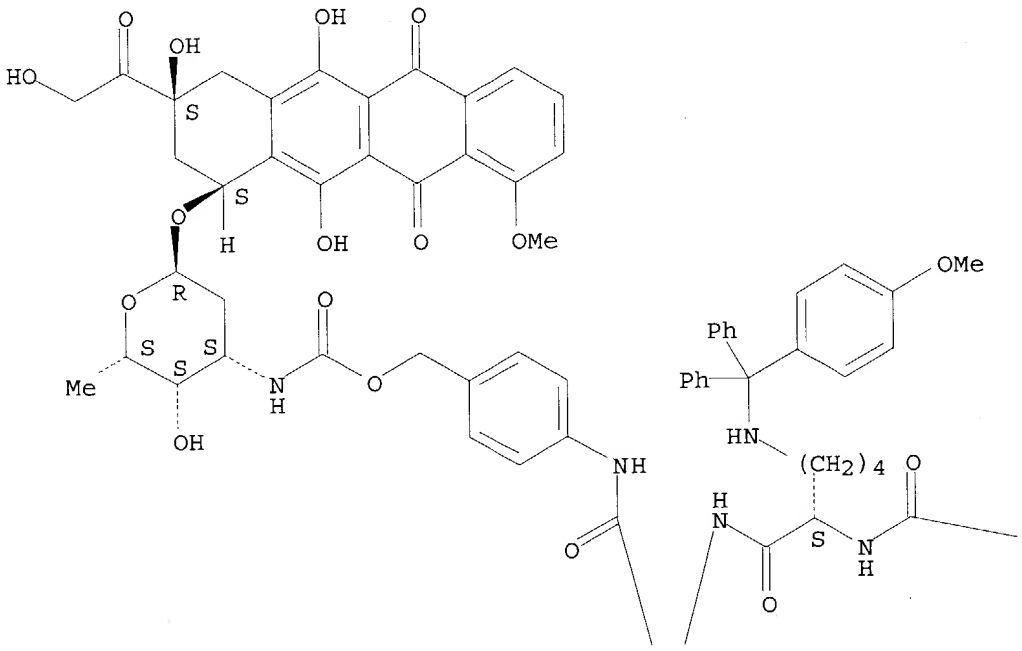
CRN 79-43-6
CMF C2 H2 Cl2 O2



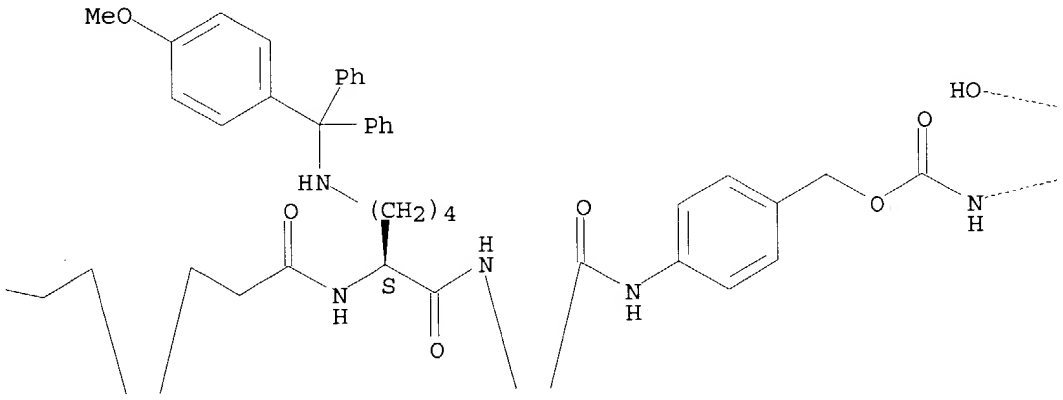
RN 207613-67-0 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

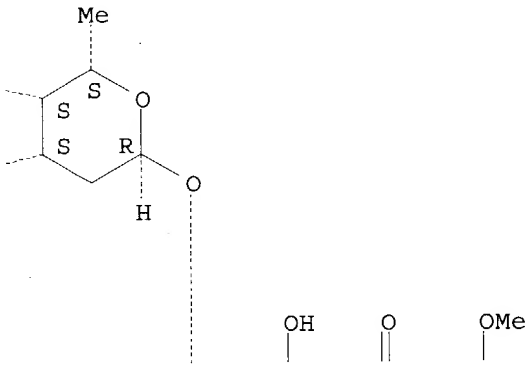


PAGE 1-B



Searched by P. Ruppel

PAGE 1-C



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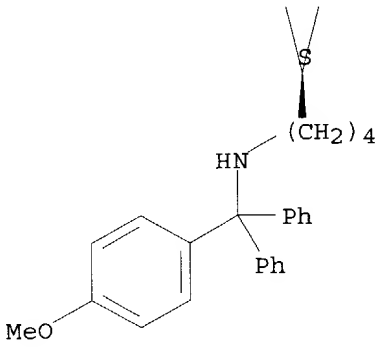

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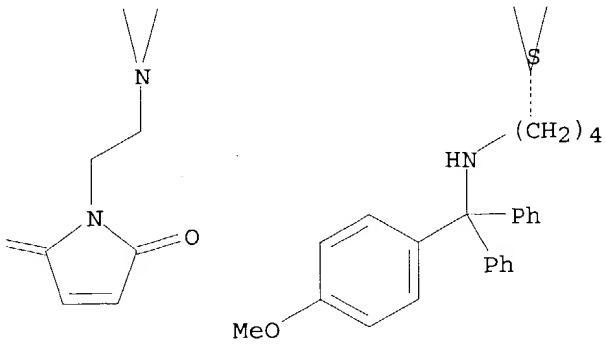
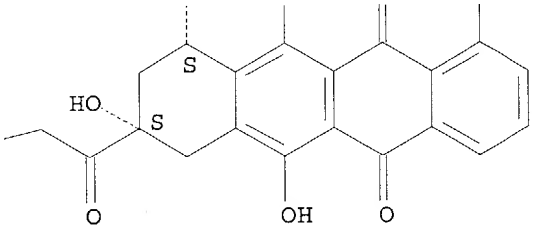


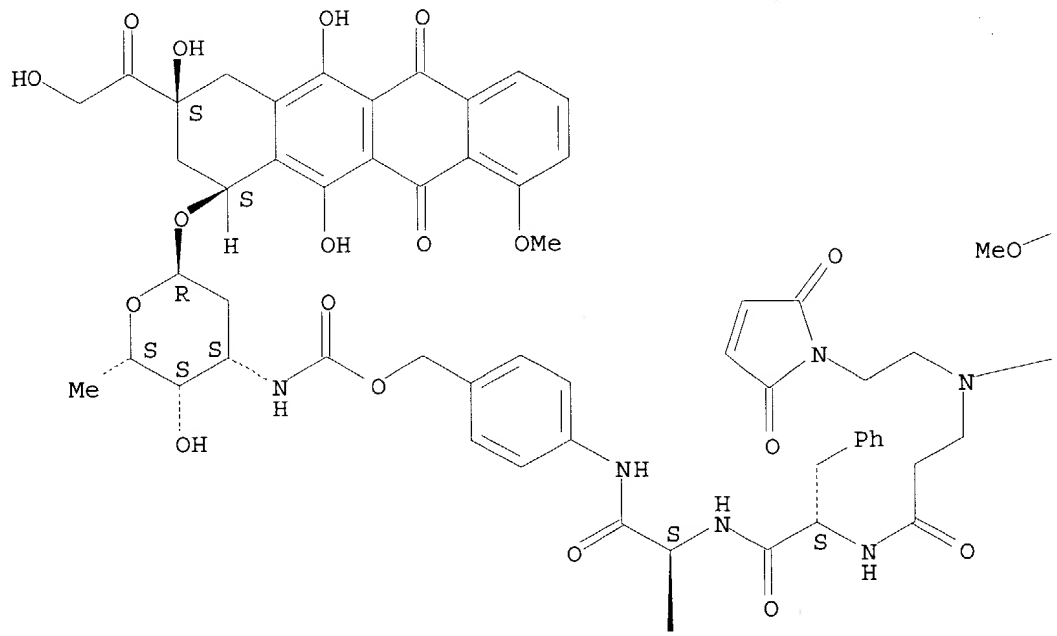
PAGE 2-C



RN 207613-68-1 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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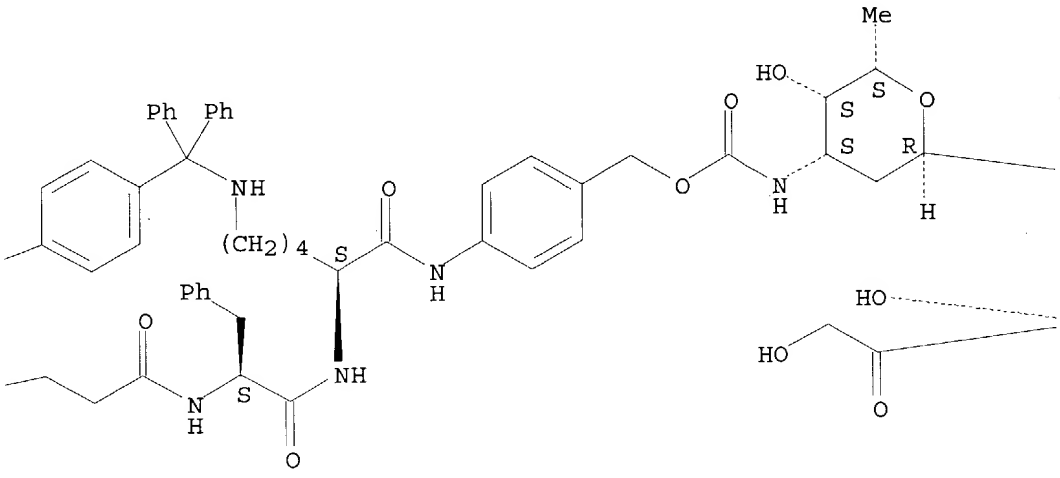

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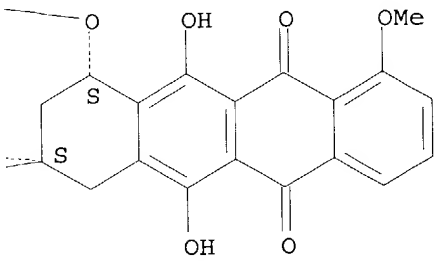

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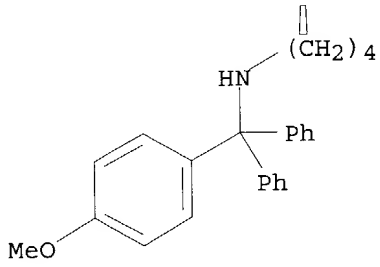
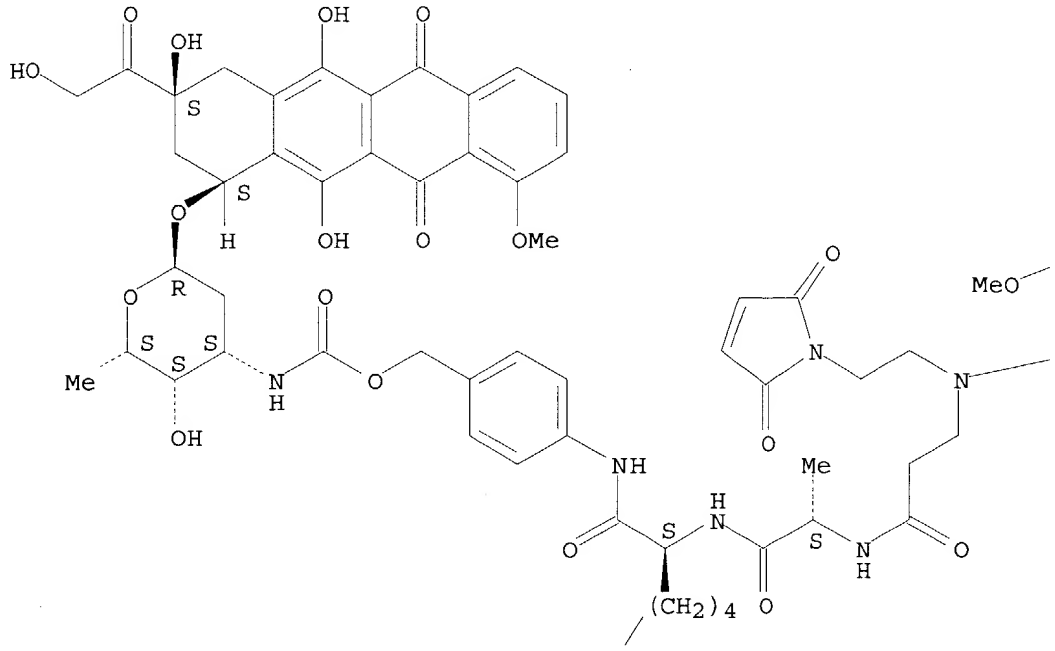


RN 207613-69-2 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[L-alanyl-N-[4-(hydroxymethyl)phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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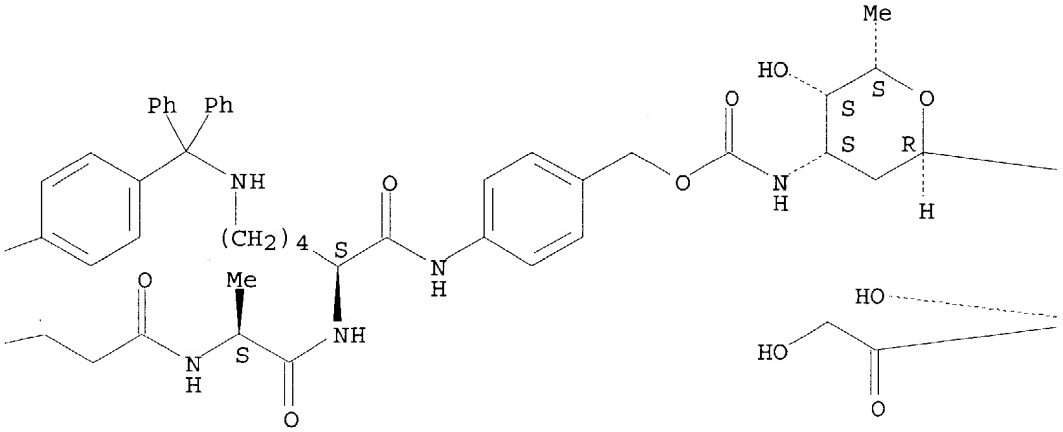

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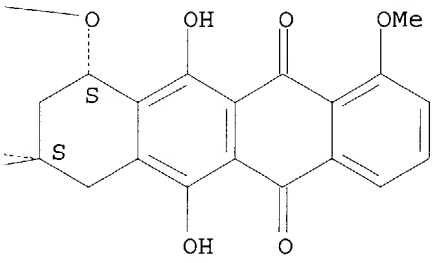

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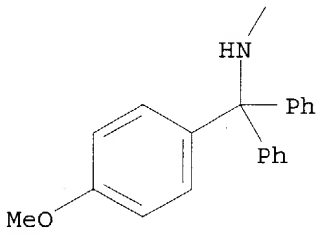


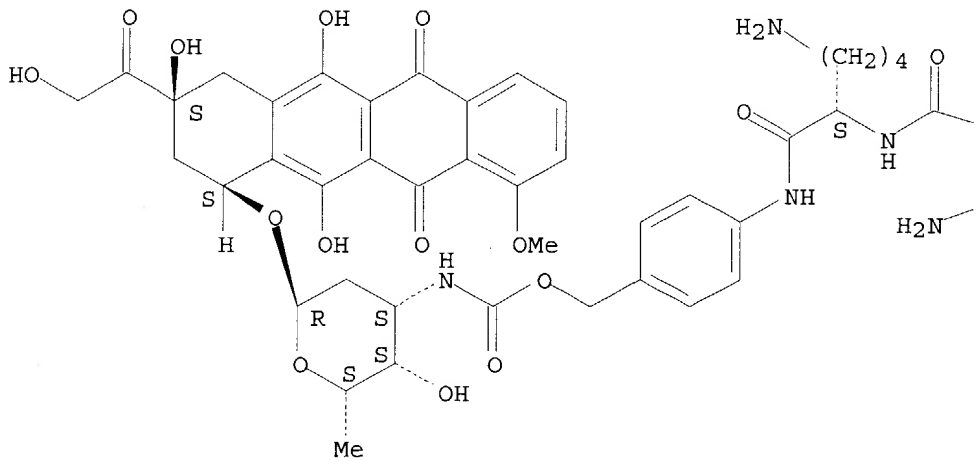
RN 207613-71-6 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[L-lysyl-N-[4-(hydroxymethyl)phenyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, pentakis(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

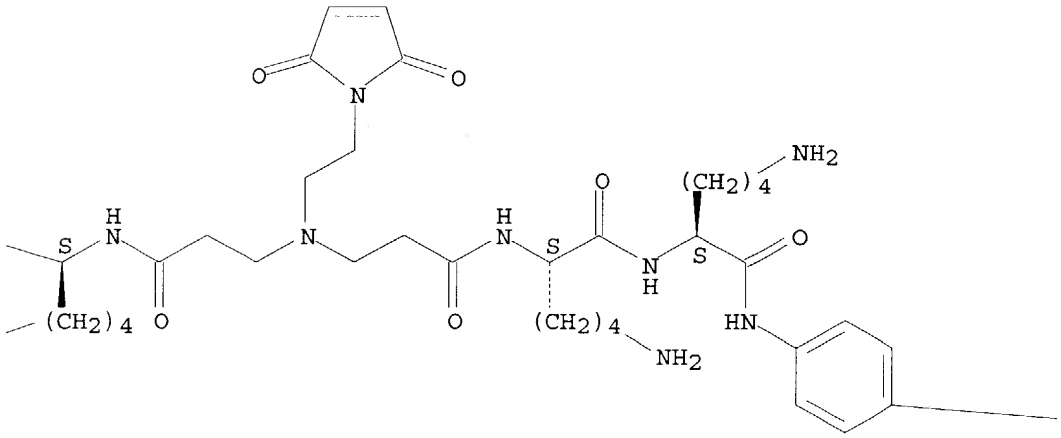
CRN 207613-70-5
CMF C106 H132 N14 O34

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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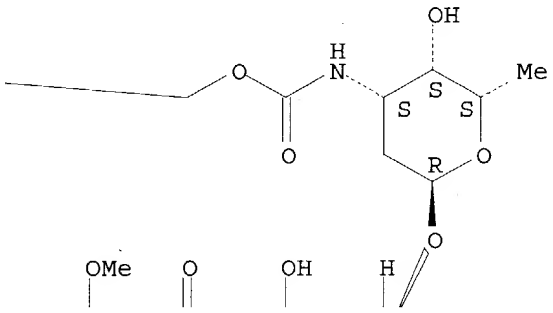

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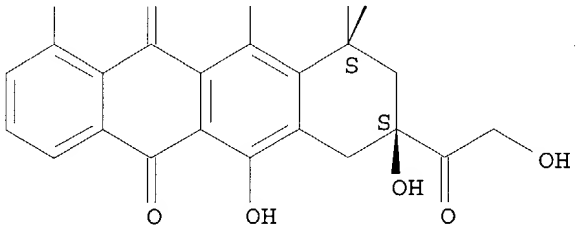
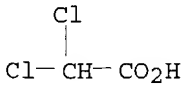


CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2



RN 207613-73-8 HCAPLUS
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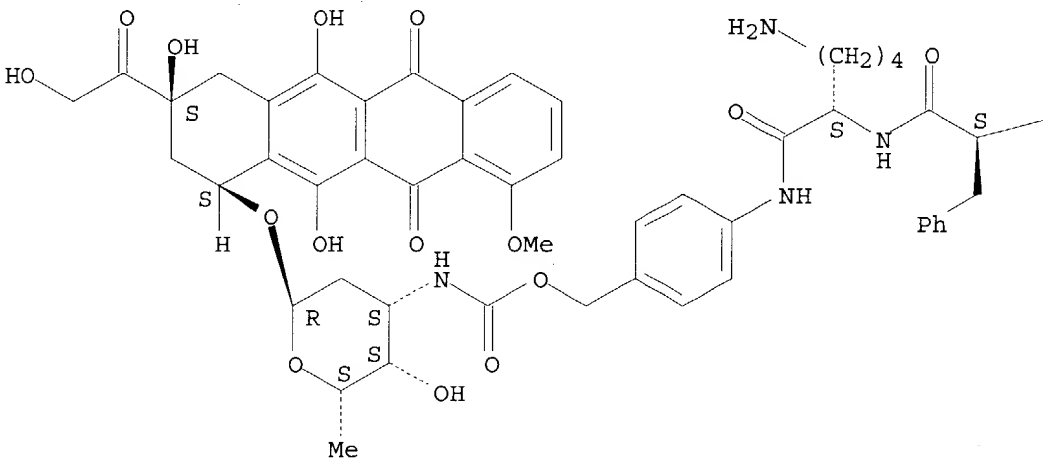
CM 1

CRN 207613-72-7
CMF C112 H126 N12 O34

Absolute stereochemistry.

PAGE 1-A



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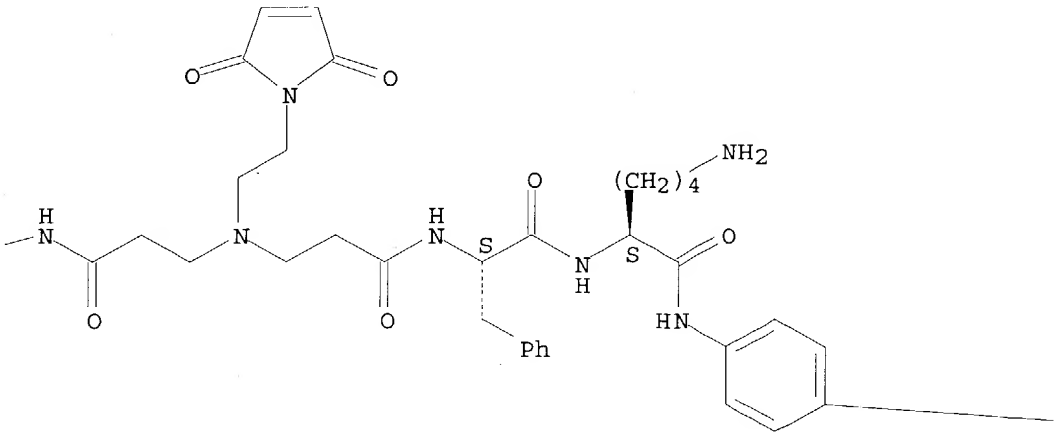

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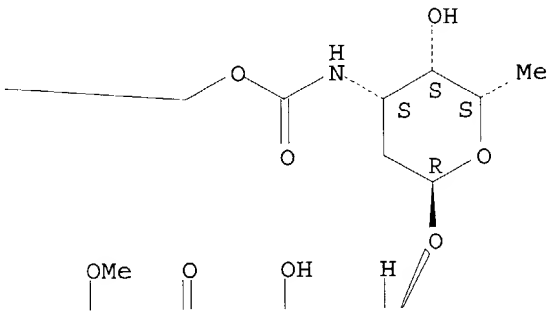

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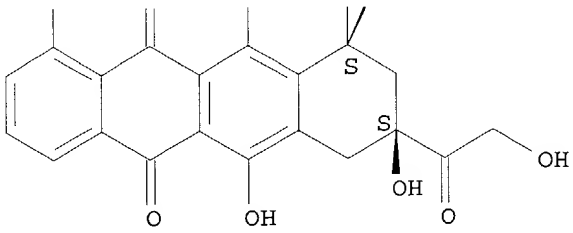
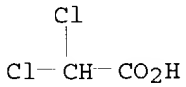


CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2



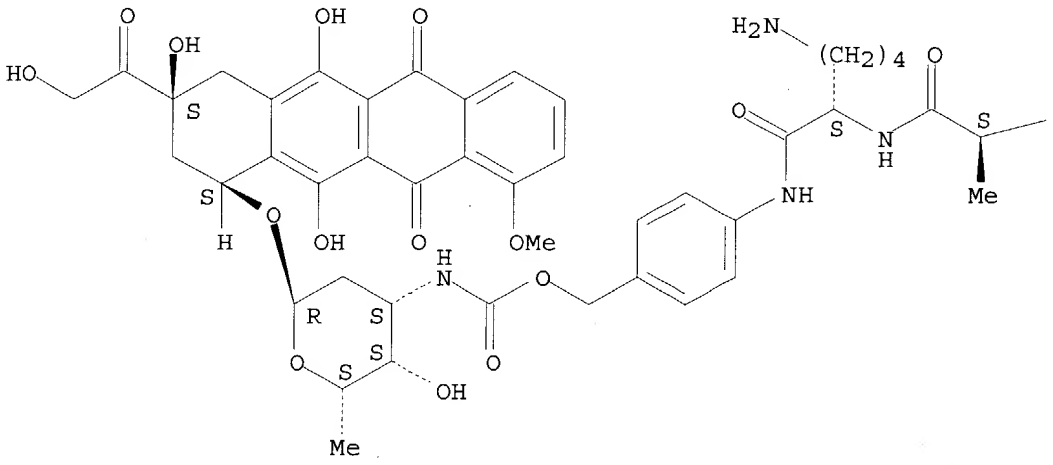
RN 207613-75-0 HCAPLUS
CN L-Lysinamide, 1,1'-[[[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]imino]bis(1-oxo-3,1-propanediyl)]bis[L-alanyl-N-[4-(hydroxymethyl)phenyl]-, diester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, tris(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 207613-74-9
CMF C100 H118 N12 O34

Absolute stereochemistry.

PAGE 1-A



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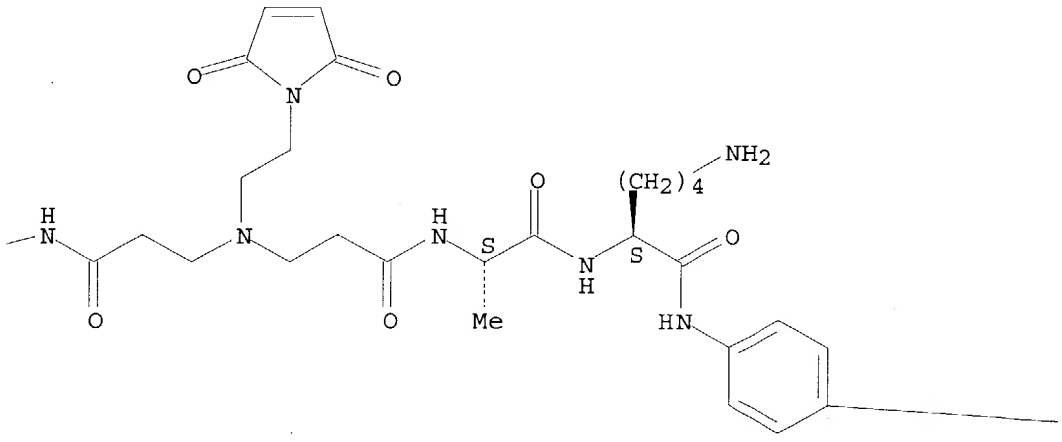

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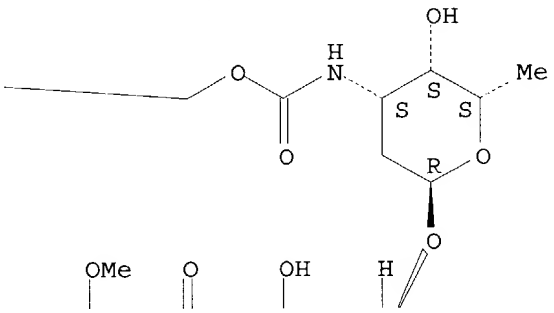

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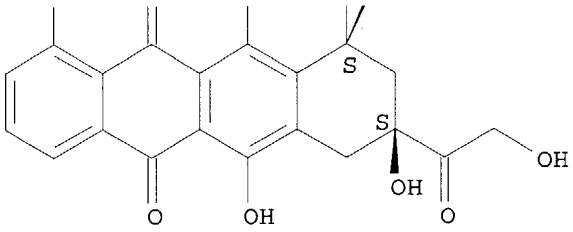
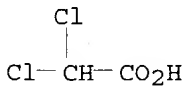


CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2



RN 207613-84-1 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with

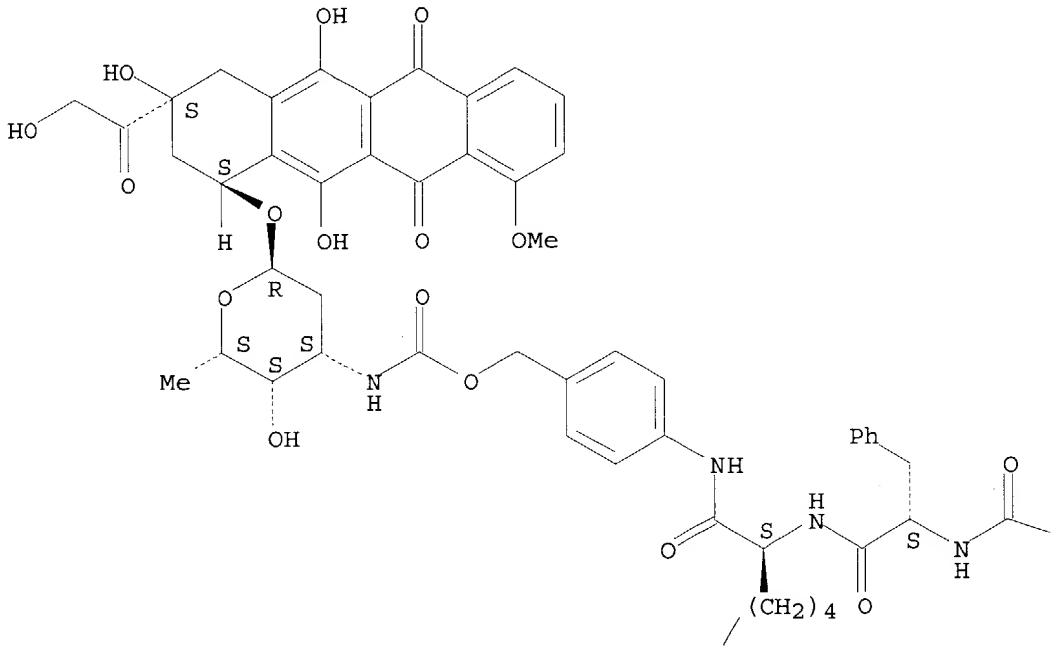
(8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, bis(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 207613-83-0
CMF C110 H122 N12 O34

Absolute stereochemistry.

PAGE 1-A



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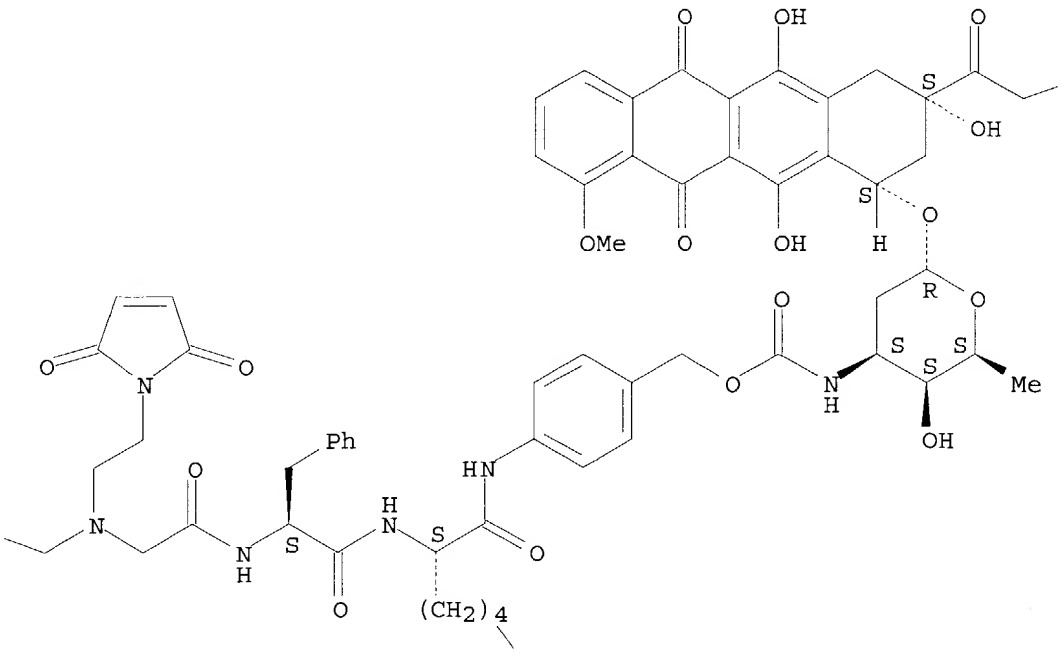


PAGE 1-C

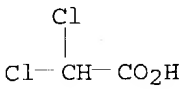
PAGE 2-A

PAGE 2-B

CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2

Searched by P. Ruppel



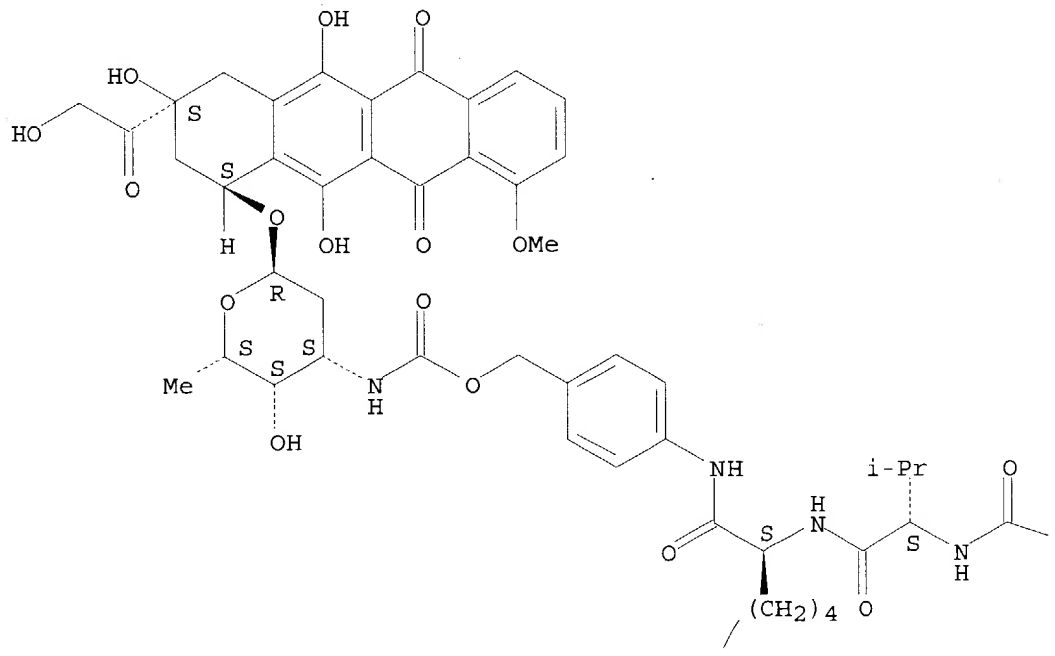
RN 207613-86-3 HCAPLUS
CN L-Lysinamide, N-(carboxymethyl)-N-[2-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)ethyl]glycyl-L-valyl-N-[4-(hydroxymethyl)phenyl]-, 3-ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, (1→1')-amide with L-valyl-N-[4-(hydroxymethyl)phenyl]-L-lysinamide ester with (8S,10S)-10-[[3-(carboxyamino)-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-5,12-naphthacenedione, bis(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 207613-85-2
CMF C102 H122 N12 O34

Absolute stereochemistry.

PAGE 1-A



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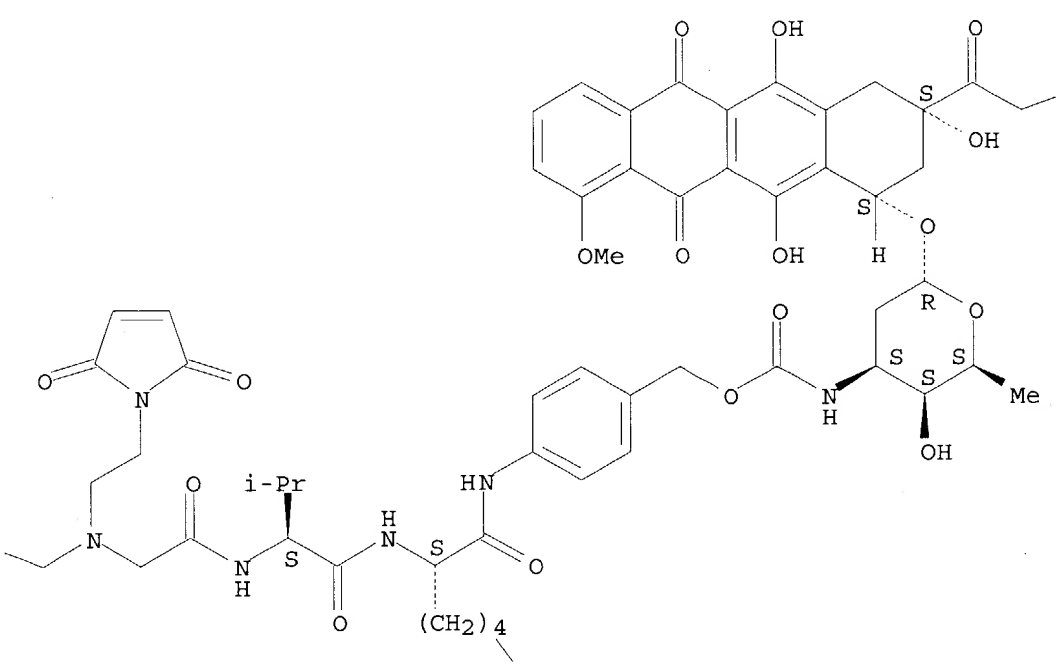


PAGE 1-C

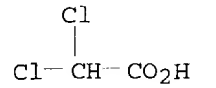
PAGE 2-A

PAGE 2-B

CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2

Searched by P. Ruppel



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:260097 HCAPLUS
DOCUMENT NUMBER: 122:38862
TITLE: Lysosomal enzyme-cleavable antitumor drug **conjugates**
INVENTOR(S): Firestone, Raymond Armand; Dubowchik, Gene Michael
PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
SOURCE: Eur. Pat. Appl., 84 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 624377	A2	19941117	EP 1994-107501	19940513
EP 624377	A3	19951115		
EP 624377	B1	20020123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 6214345	B1	20010410	US 1993-62366	19930514
CA 2123363	AA	19941115	CA 1994-2123363	19940511
AU 9463026	A1	19941117	AU 1994-63026	19940512
AU 687795	B2	19980305		
FI 9402237	A	19941115	FI 1994-2237	19940513
NO 9401819	A	19941115	NO 1994-1819	19940513
HU 66485	A2	19941128	HU 1994-1507	19940513
CN 1100426	A	19950322	CN 1994-107589	19940513
CN 1117760	B	20030813		
AT 212236	E	20020215	AT 1994-107501	19940513
PT 624377	T	20020731	PT 1994-94107501	19940513
ES 2170755	T3	20020816	ES 1994-107501	19940513
JP 07070175	A2	19950314	JP 1994-101389	19940516

PRIORITY APPLN. INFO.: US 1993-62366 A 19930514
OTHER SOURCE(S): CASREACT 122:38862; MARPAT 122:38862

AB An antitumor drug is targeted to the site of tumor cells in a warm-blooded animal by administration as a conjugate L[AYmZmXnWn]D (L = cell-specific ligand; A = acyl; Y, Z = amino acid; X, W = spacer; D = drug functionalized with amino, OH, SH, CO2H, CHO, or ketone group for attachment to the spacer; m = 1-6; n = 0, 1), the peptide linker being cleavable by a lysosomal proteinase such as cathepsin B, C, or D to release the antitumor drug in pharmacol. active form selectively at the tumor site. These conjugates show less systemic toxicity than conjugates which rely on simple acid hydrolysis for drug release. X and W are self-immolating spacers which are spontaneously cleaved from the drug moiety after enzymic cleavage of the peptide. Thus, a monoclonal antibody to antigen BR96, which is expressed by L2987 human lung carcinoma, was coupled to maleimidocaproyl-Phe-Lys-p-aminobenzylcarbamoyldoxorubicin (preparation given). This conjugate was highly cytotoxic against L2987 cells in vitro and in xenografts.

IT **159857-68-8DP**, antibody **conjugates 159858-32-9DP**

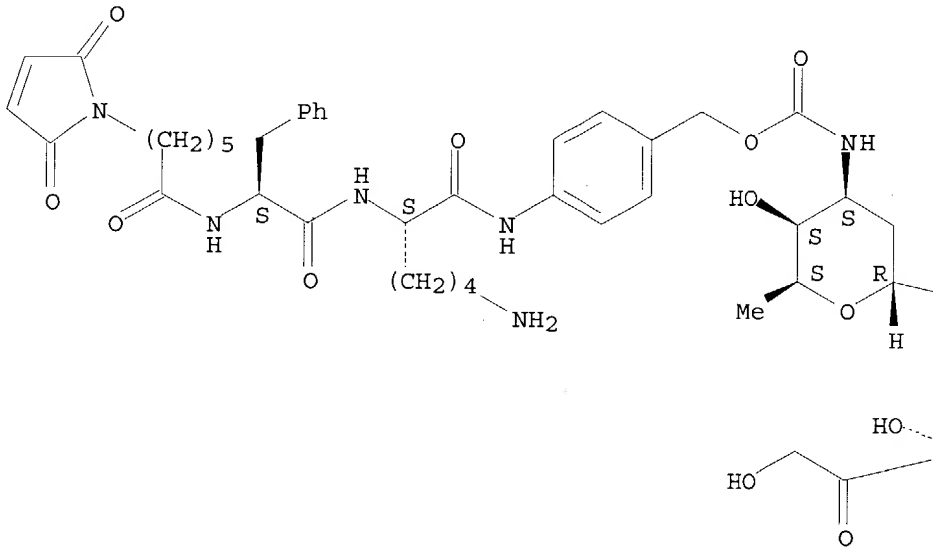
, reaction products with succinimidyl iodoacetamidobenzoate and SPDP, antibody **conjugates**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(lysosomal enzyme-cleavable antitumor drug **conjugates**)

RN 159857-68-8 HCAPLUS

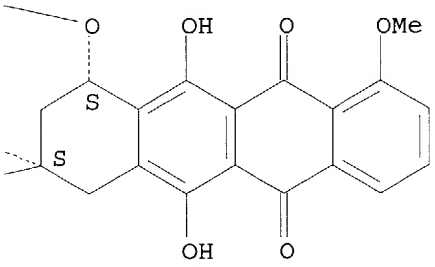
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



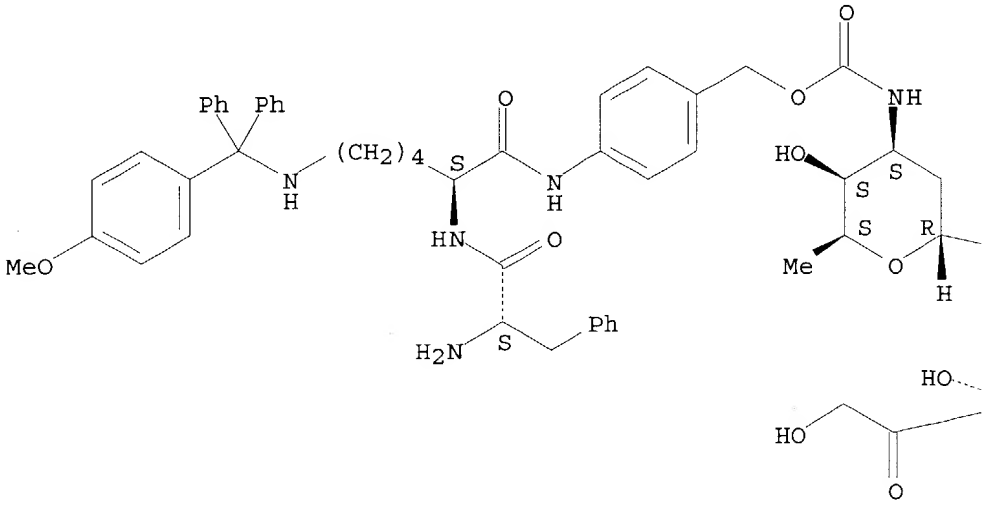
PAGE 1-B



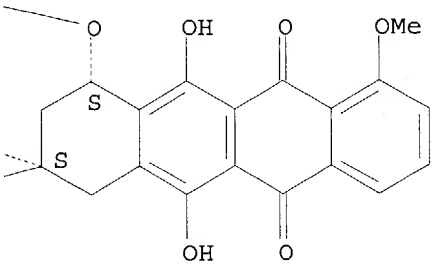
RN 159858-32-9 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N6-[(4-methoxyphenyl)diphenylmethyl]-N2-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



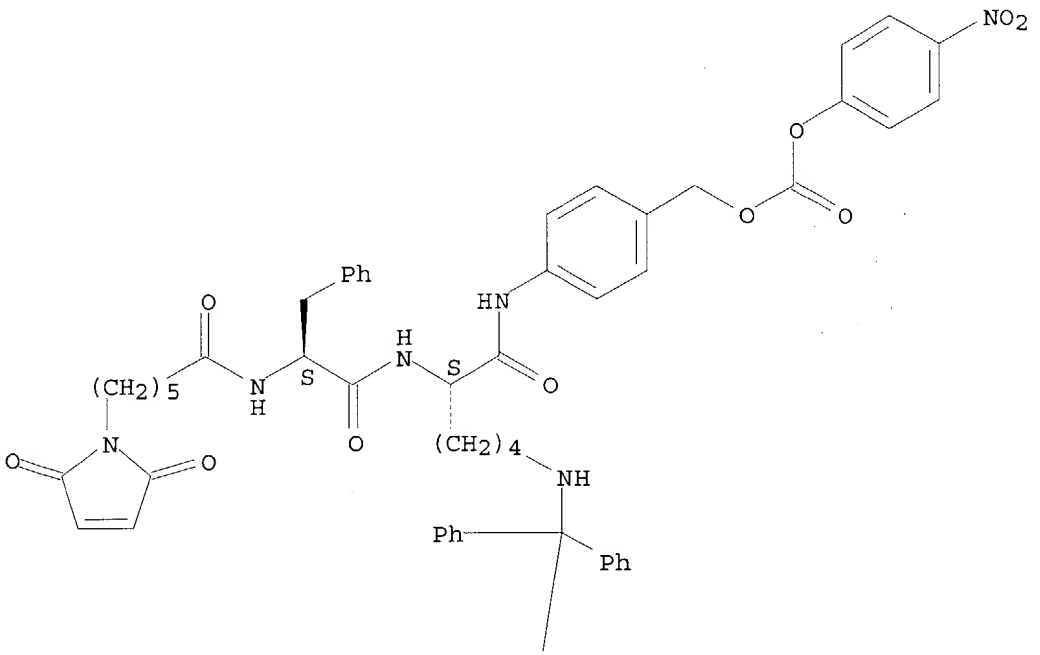
IT **159857-66-6P 159857-67-7P 159857-69-9P**
159857-70-2P 159857-72-4P 159857-74-6P
159857-76-8P 159857-81-5P 159857-82-6P
159857-83-7P 159857-90-6P 159857-91-7P
159857-92-8P 159857-95-1P 159857-96-2P
159857-97-3P 159858-03-4P 159858-04-5P
159858-05-6P 159858-08-9P 159858-09-0P
159858-10-3P 159858-11-4P 159858-15-8P
159858-16-9P 159858-17-0P 159858-18-1P
159858-19-2P 159858-27-2P 159858-28-3P
159858-29-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(lysosomal enzyme-cleavable antitumor drug **conjugates**)

RN 159857-66-6 HCAPLUS

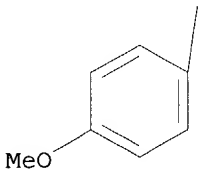
CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



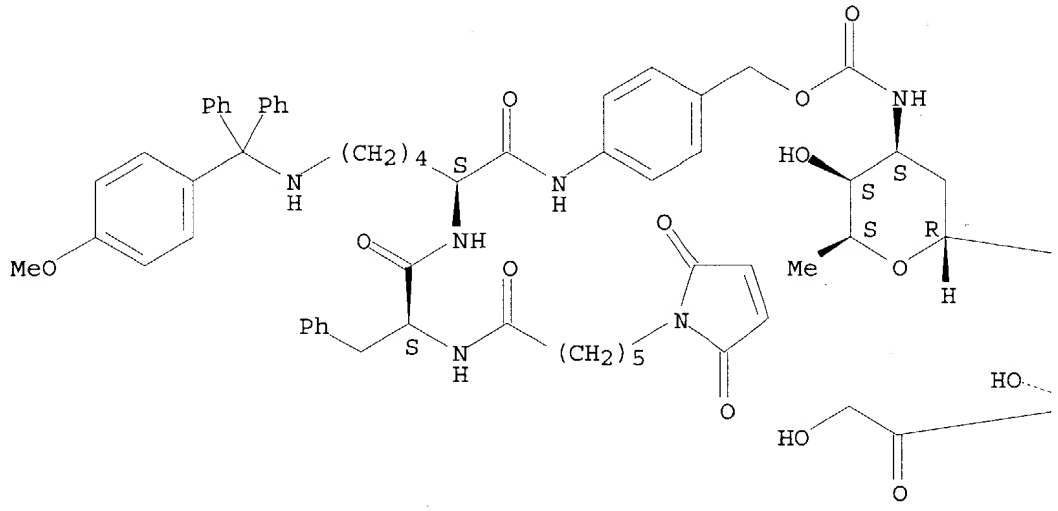
PAGE 2-A



RN 159857-67-7 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N6-[(4-methoxyphenyl)diphenylmethyl]-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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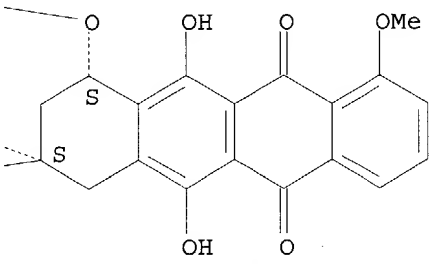


RN 159857-69-9 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,,10S)-, mono(dichloroacetate) (salt) (9CI) (CA INDEX NAME)

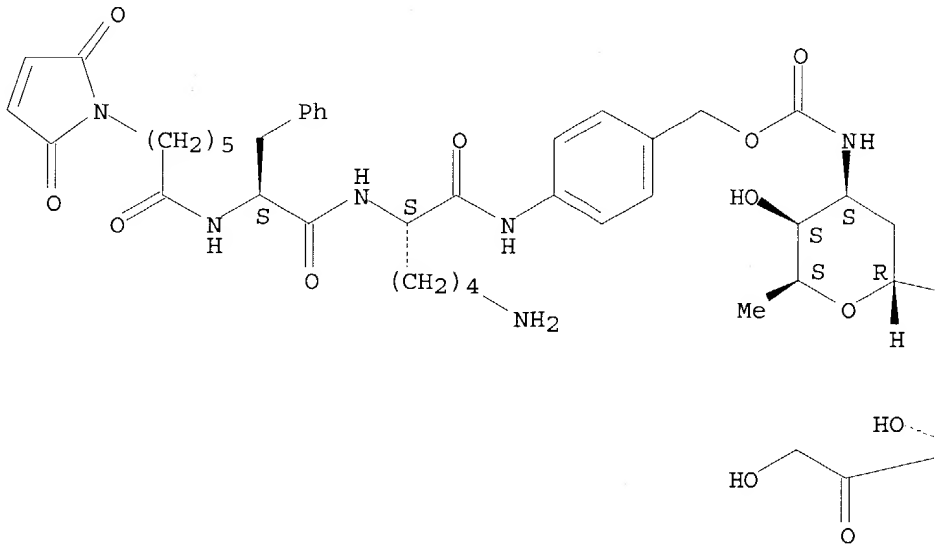
CM 1

CRN 159857-68-8
CMF C60 H68 N6 O18

Absolute stereochemistry.

Searched by P. Ruppel

PAGE 1-A



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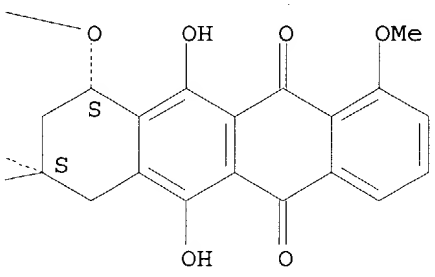
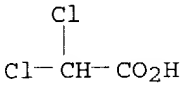


CM 2

CRN 79-43-6
CMF C2 H2 Cl2 O2

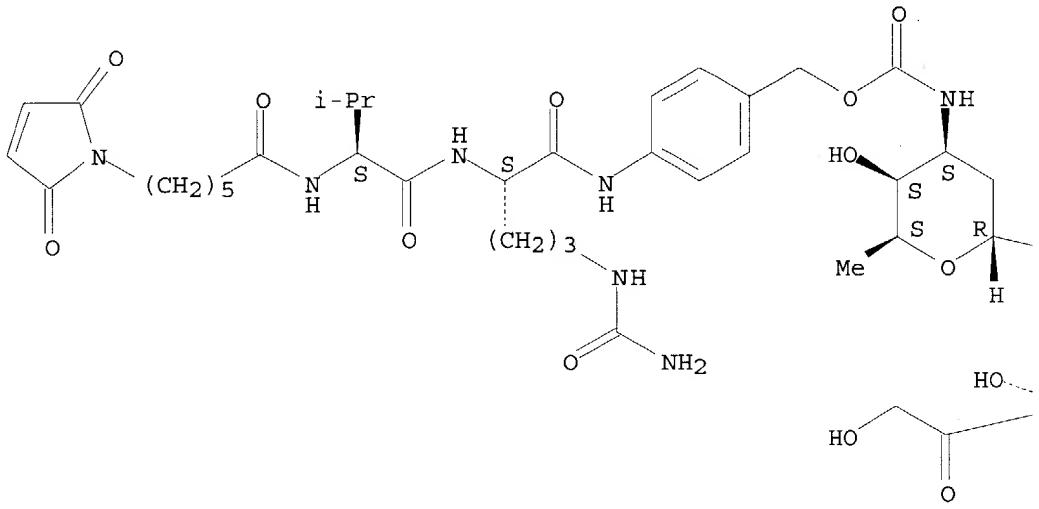
Searched by P. Ruppel



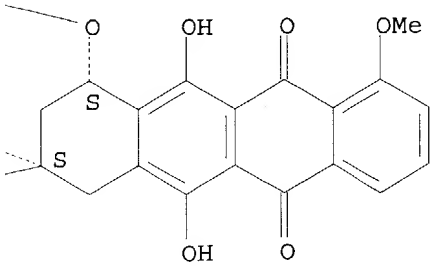
RN 159857-70-2 HCAPLUS
CN 5,12-Naphthacenedione, 10-[[3-[[[[4-[[N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-valyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

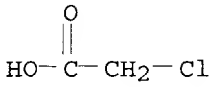


Searched by P. Ruppel

RN 159857-72-4 HCAPLUS
CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N-[4-[[[[[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]oxy]methyl]phenyl]-, [2aR-[2aα,4β,4aβ,6β,9α(2R*,3S*),11α,12.alpha.,12aα,12bα]]-, mono(chloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 79-11-8
CMF C2 H3 Cl O2



CM 2

CRN 159857-71-3
CMF C80 H90 N6 O21 . C2 H2 Cl2 O2

CM 3

CRN 194409-94-4
CMF C80 H90 N6 O21

Absolute stereochemistry.

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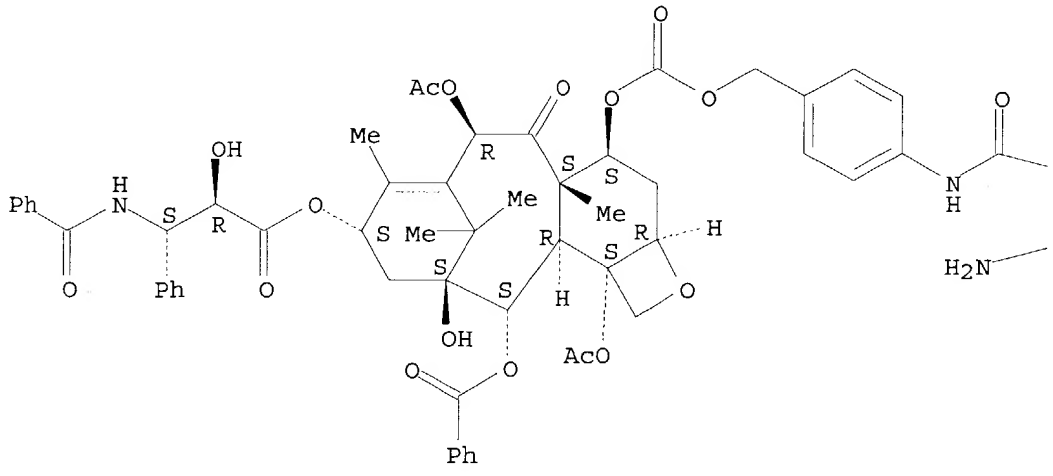
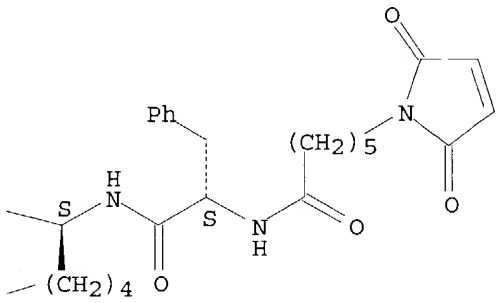
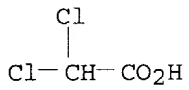


PAGE 1-B



CM 4

CRN 79-43-6
CMF C2 H2 Cl2 O2



RN 159857-74-6 HCAPLUS
CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N-[4-[[[[[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-[(ethoxycarbonyl)oxy]-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]oxy]methyl]phenyl]-, [2aR-[2aα,4β,4aβ,6.beta.,9α(2R*,3S*),11α,12α,12aα,12bα]]-, mono(chloroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 159857-73-5
CMF C83 H94 N6 O23

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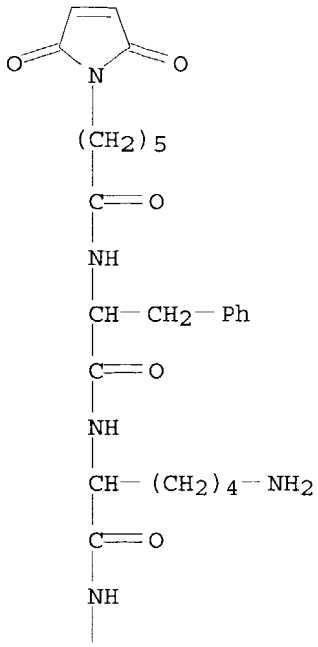
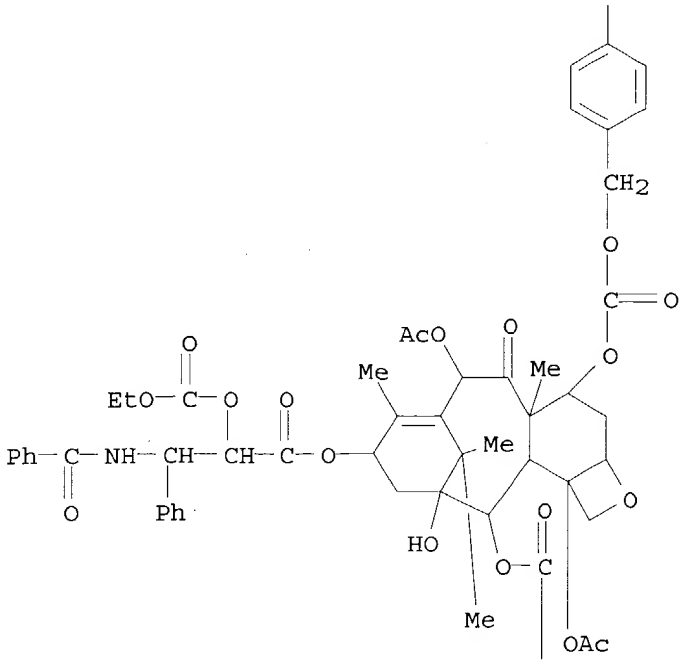


PAGE 2-A



Searched by P. Ruppel

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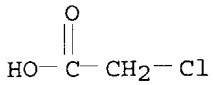
CM 2

CRN 79-11-8
CMF C2 H3 Cl O2



RN 159857-76-8 HCAPLUS
CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N-[4-[[[[6-amino-8-[[(aminocarbonyl)oxy]methyl]-1a,4,7,8,8a,8b-hexahydro-8a-methoxy-5-methyl-4,7-dioxoazirino[2',3':3,4]pyrrolo[1,2-a]indol-1(2H)-yl]carbonyl]oxy]methyl]phenyl]-, [1aS-(1aα,8β,8aα,8b.alpha.)]-, mono(chloroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 159857-75-7
CMF C48 H57 N9 O12

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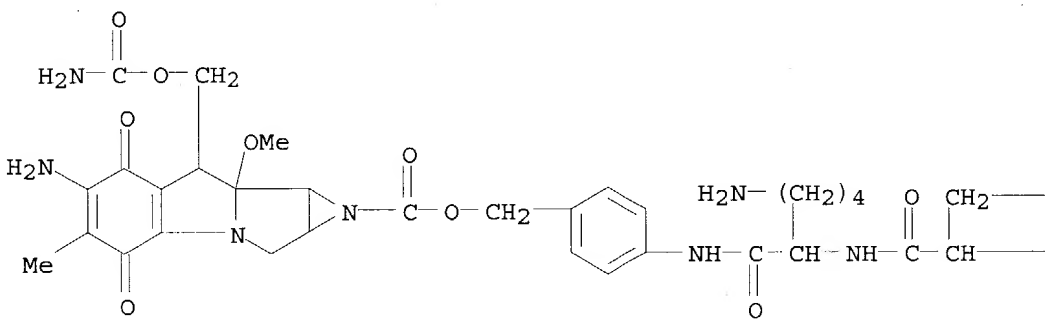

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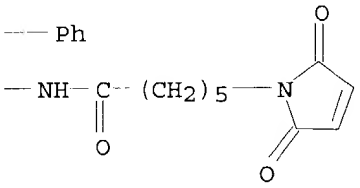
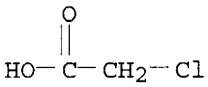


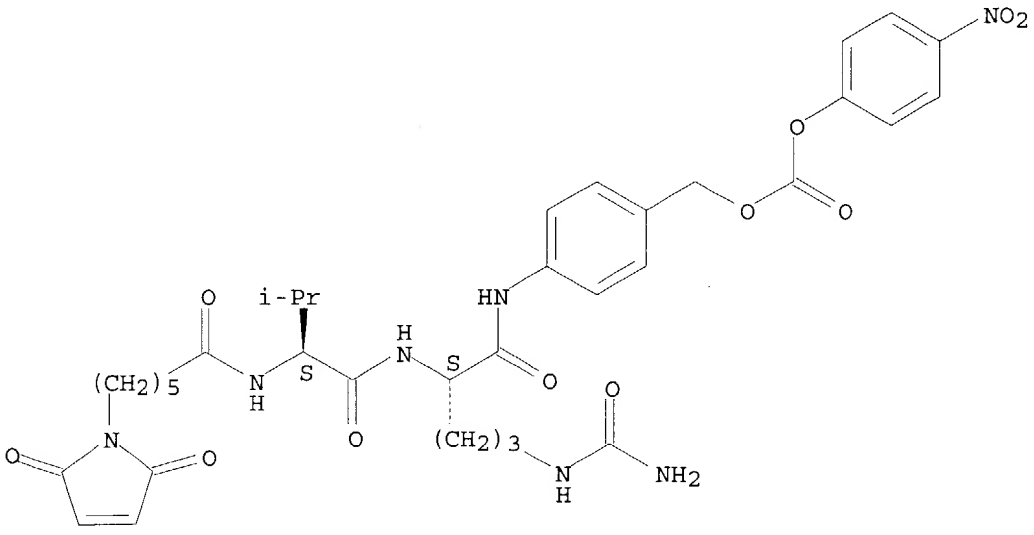
CM 2

CRN 79-11-8
CMF C2 H3 Cl O2



RN 159857-81-5 HCAPLUS
CN L-Ornithinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-valyl-N5-(aminocarbonyl)-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

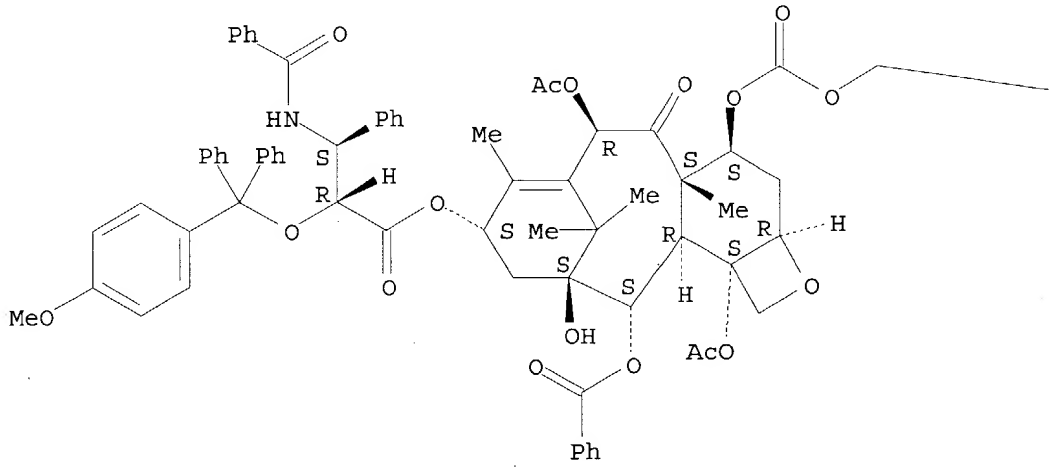


RN 159857-82-6 HCAPLUS
CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N-[4-[[[[[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-[(4-

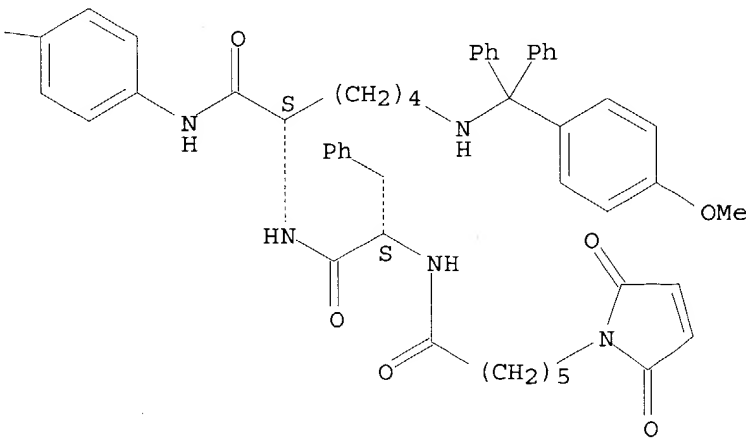
methoxyphenyl)diphenylmethoxy]-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]oxy]methyl]phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, [2aR-[2aα,4β,4aβ,6β,9α(2R*,3S*),11α,12.alpha.,12aα,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 159857-83-7 HCAPLUS

CN L-Lysinamide, N-[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]-L-phenylalanyl-N-[4-[[[[6-amino-8-[[(aminocarbonyl)oxy]methyl]-1a,4,7,8,8a,8b-hexahydro-8a-methoxy-5-methyl-4,7-dioxoazirino[2',3':3,4]pyrrolo[1,2-a]indol-1(2H)-yl]carbonyl]oxy]methyl]phenyl]-N6-[(4-methoxyphenyl)diphenylmethyl]-, [1aS-(1aα,8β,8aα,8bα)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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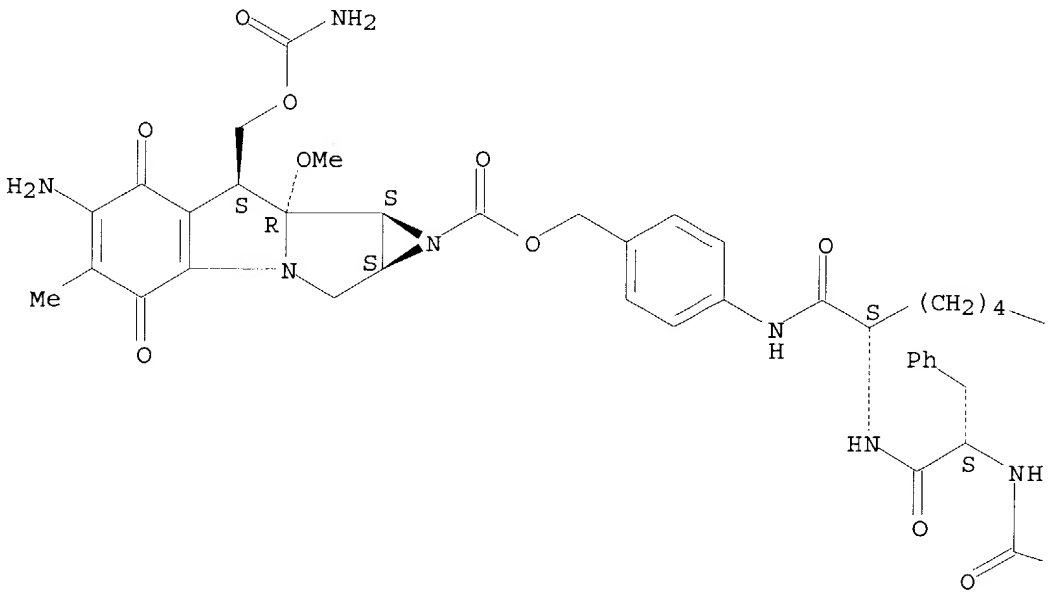

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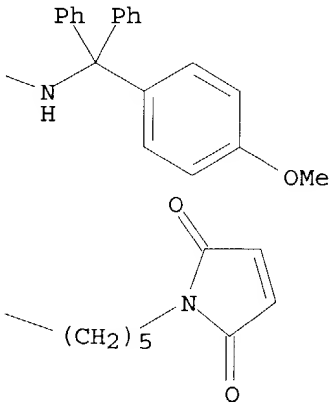
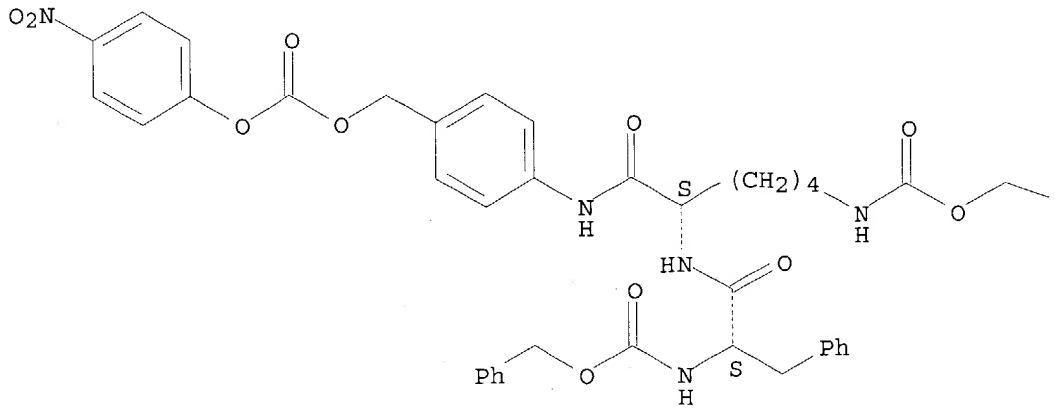


RN 159857-90-6 HCAPLUS
CN L-Lysinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-N6-[(2-propenyloxy)carbonyl]- (9CI) (CA INDEX NAME)

Searched by P. Ruppel

Absolute stereochemistry.

PAGE 1-A



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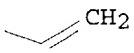

RN 159857-91-7 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N6-[(2-propenyloxy)carbonyl]-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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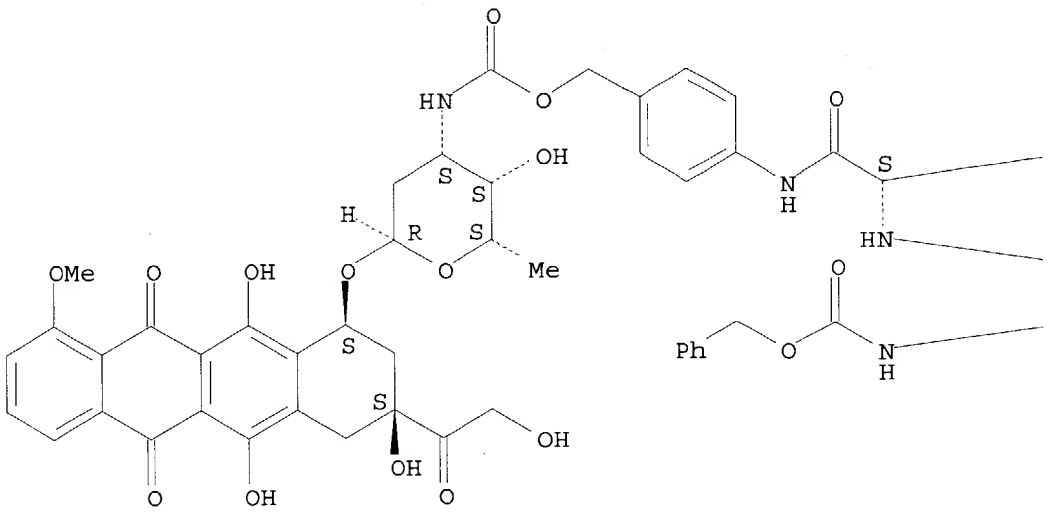

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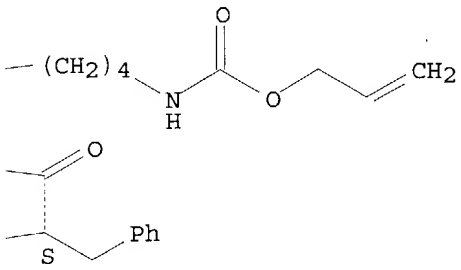
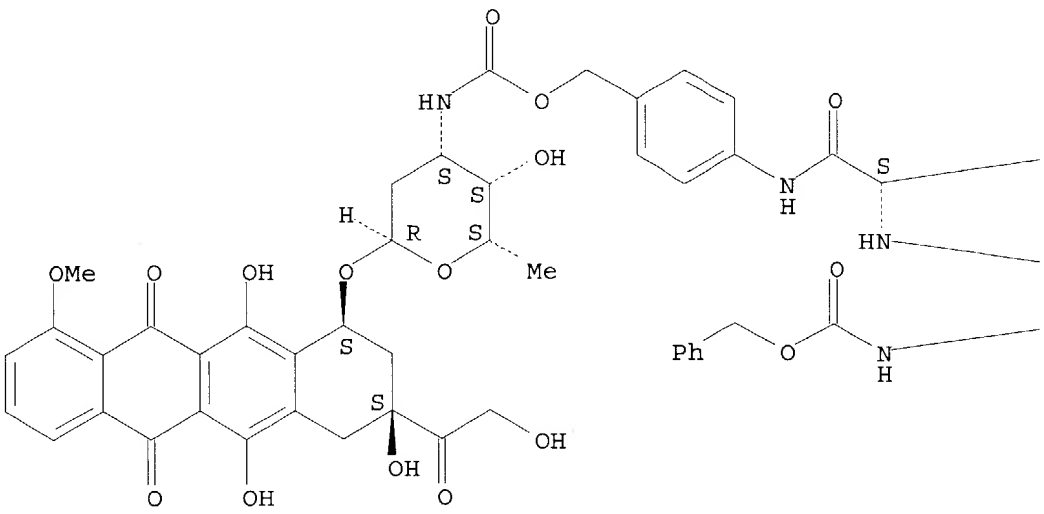


RN 159857-92-8 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, monohydrochloride, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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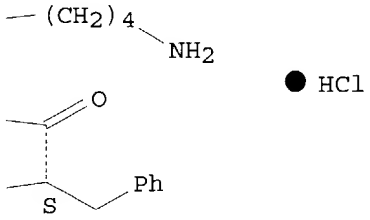

RN 159857-95-1 HCAPLUS
CN L-Lysinamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-N6-[(2-propenyloxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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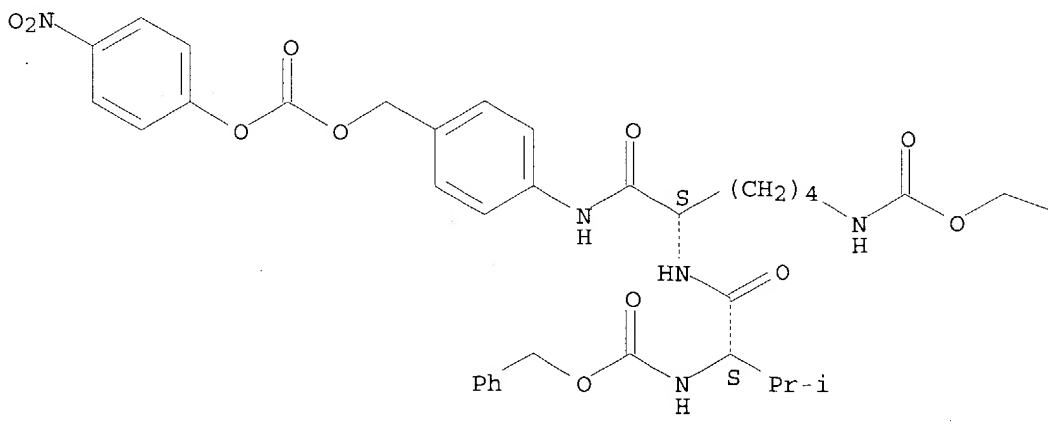

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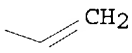
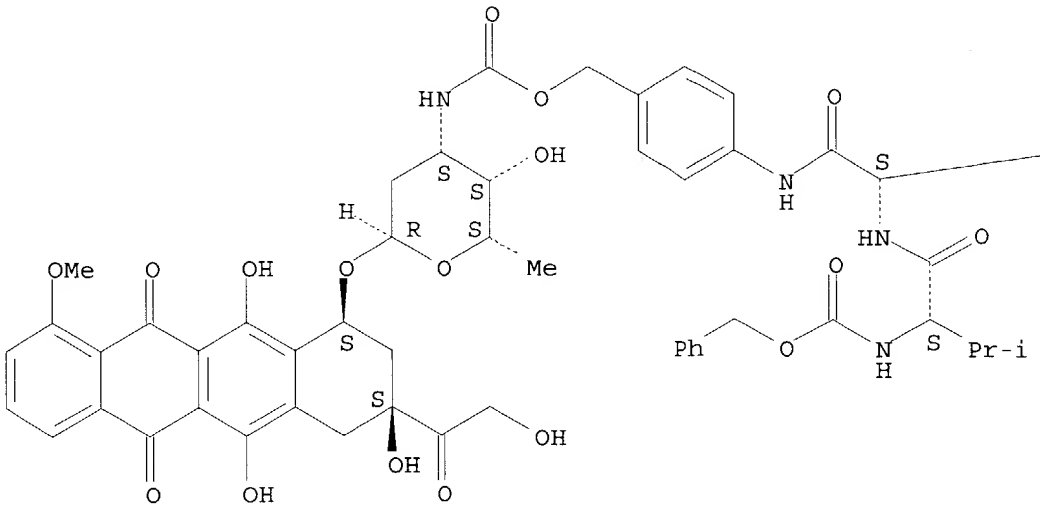


RN 159857-96-2 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-valyl-N6-[(2-propenyloxy)carbonyl]-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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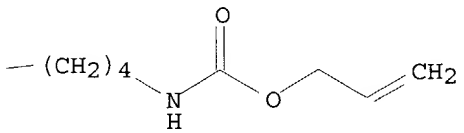
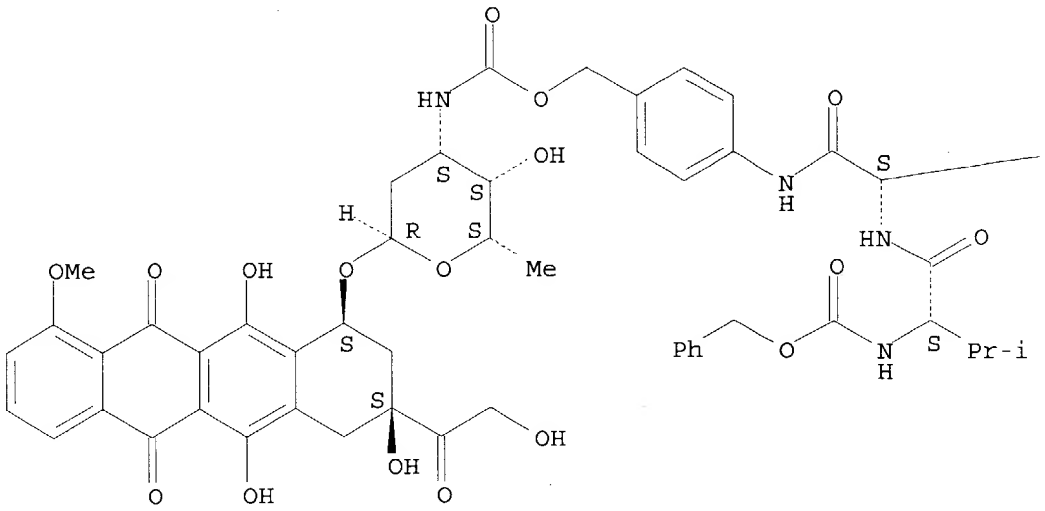


RN 159857-97-3 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-valyl-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, monohydrochloride, (8S,10S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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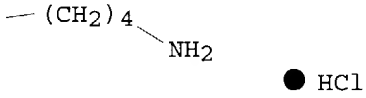

RN 159858-03-4 HCAPLUS
CN L-Lysinamide, N-[(2-propenyloxy)carbonyl]-D-phenylalanyl-L-phenylalanyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-N6-[(2-propenyloxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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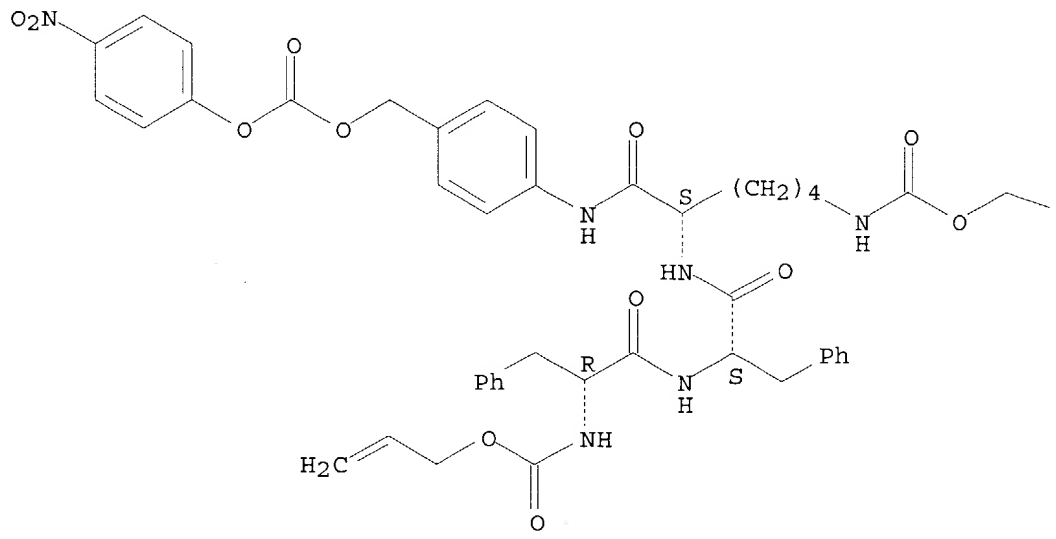

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RN 159858-04-5 HCAPLUS
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N-[(2-propenyloxy)carbonyl]-D-phenylalanyl-L-phenylalanyl-N6-[(2-propenyloxy)carbonyl]-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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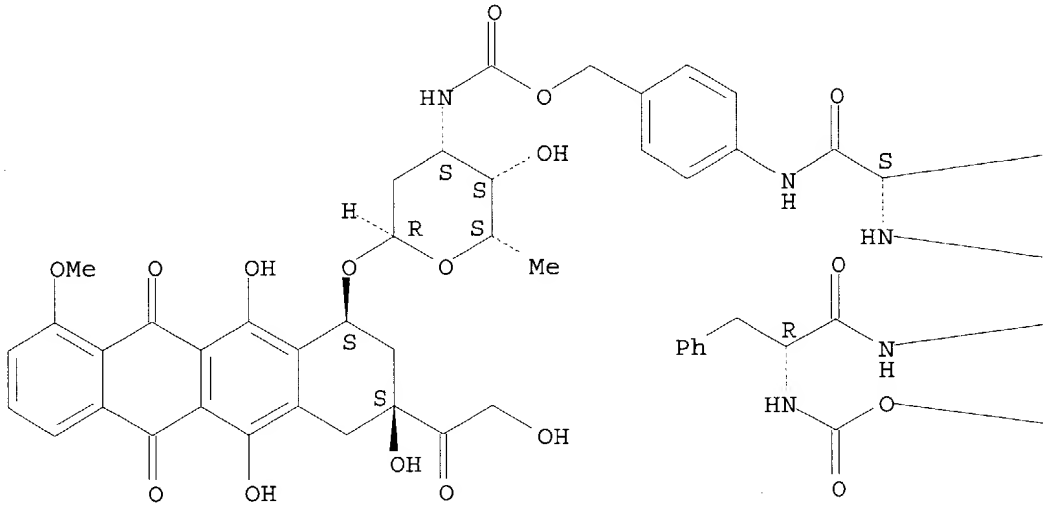

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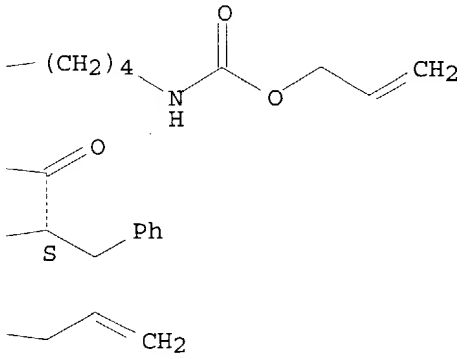

RN 159858-05-6 HCAPLUS

CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[[[4-[[N2-(N-D-phenylalanyl-L-phenylalanyl)-L-lysyl]amino]phenyl]methoxy]carbonyl]amino]-α-L-lyxo-hexopyranosyl]oxy]-, dihydrochloride, (8S-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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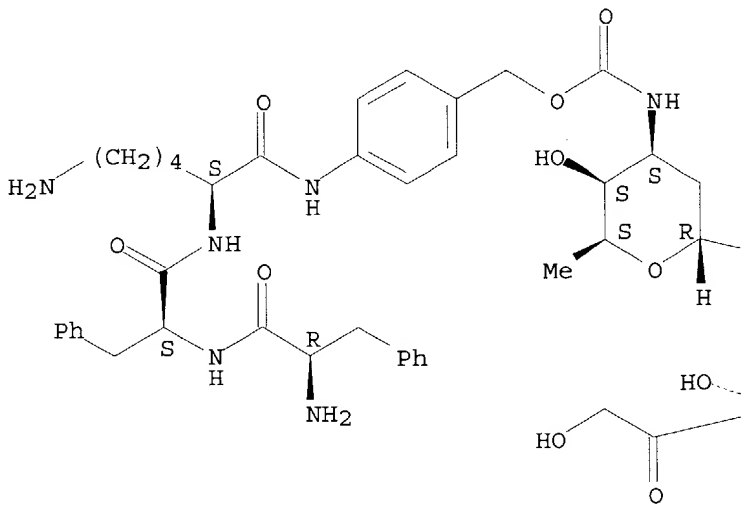

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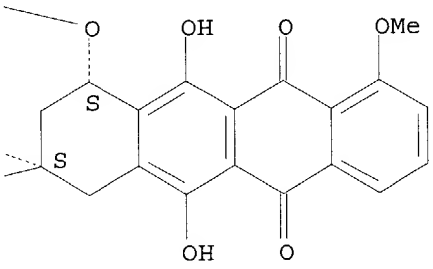
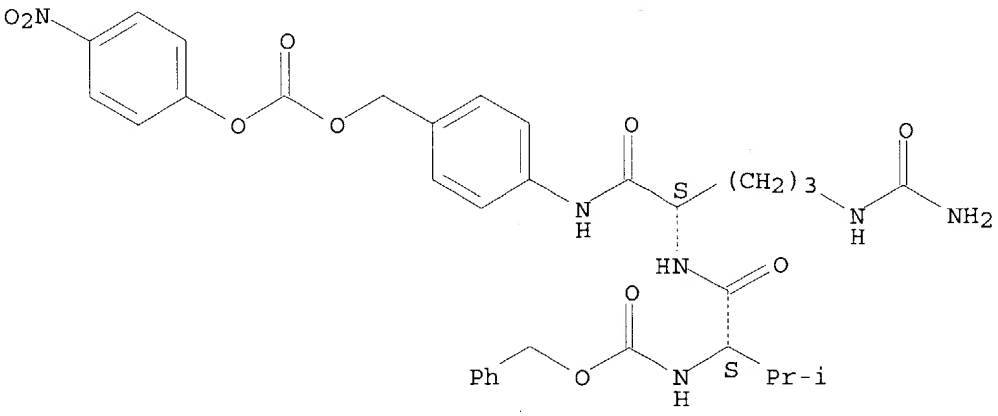
●2 HCl



RN 159858-08-9 HCAPLUS
CN L-Ornithinamide, N-[(phenylmethoxy)carbonyl]-L-valyl-N5-(aminocarbonyl)-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

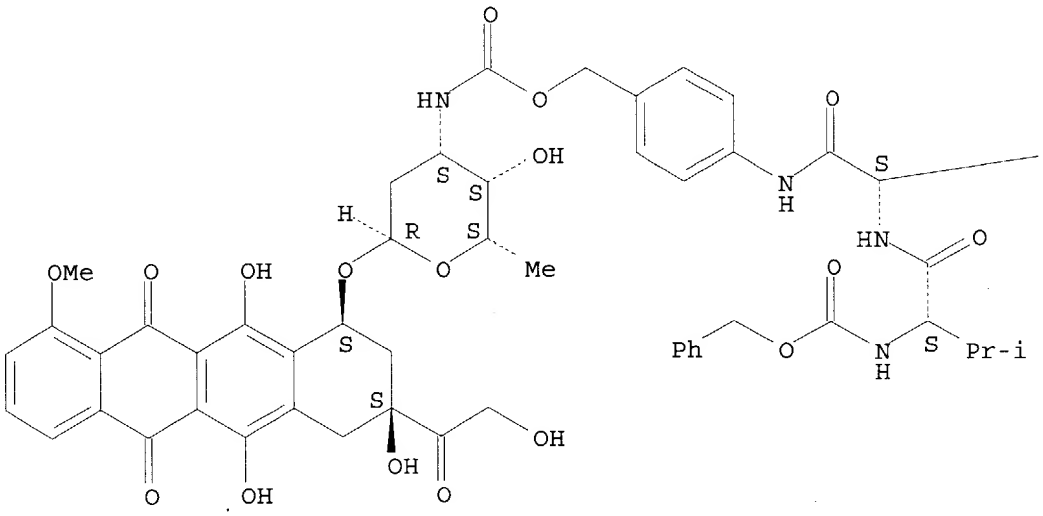
Absolute stereochemistry.



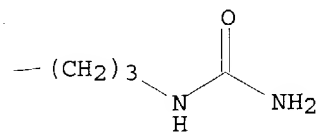
RN 159858-09-0 HCAPLUS
CN 5,12-Naphthacenedione, 10-[[3-[[[[4-[[N-[(phenylmethoxy)carbonyl]-L-valyl-N5-(aminocarbonyl)-L-ornithyl]amino]phenyl]methoxy]carbonyl]amino]-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl]oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



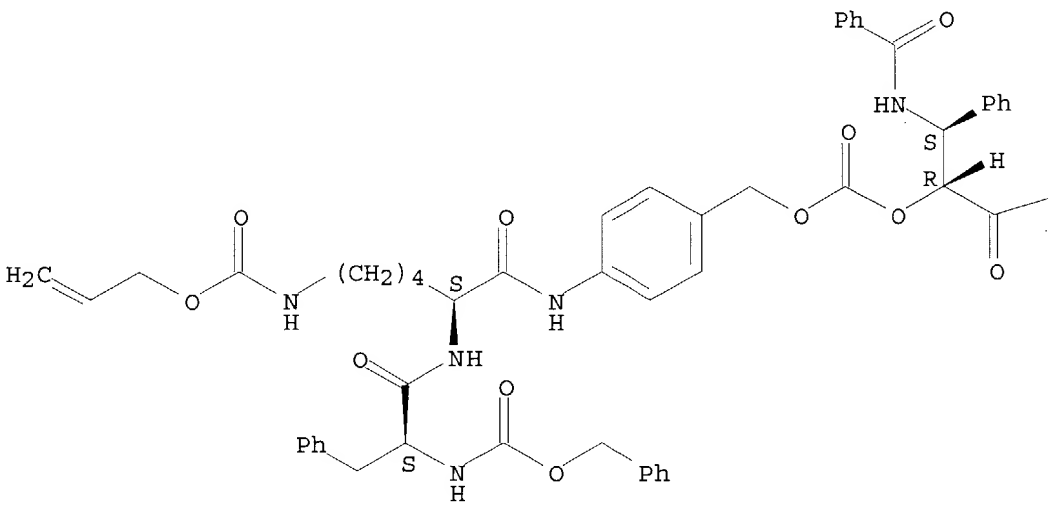
PAGE 1-B



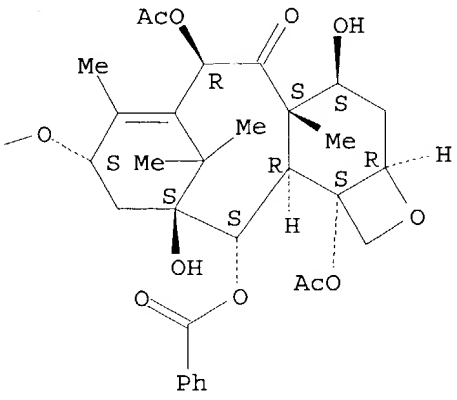
RN 159858-10-3 HCAPLUS
CN L-Lysinamide, N-[(phenylmethoxy)carbonyl]-L-phenylalanyl-N-[4-[[[[(1R)-2-[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl]oxy]-1-[(S)-(benzoylamino)phenylmethyl]-2-oxoethoxy]carbonyl]oxy]methyl]phenyl]-N6-[(2-propenyloxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RN 159858-11-4 HCAPLUS
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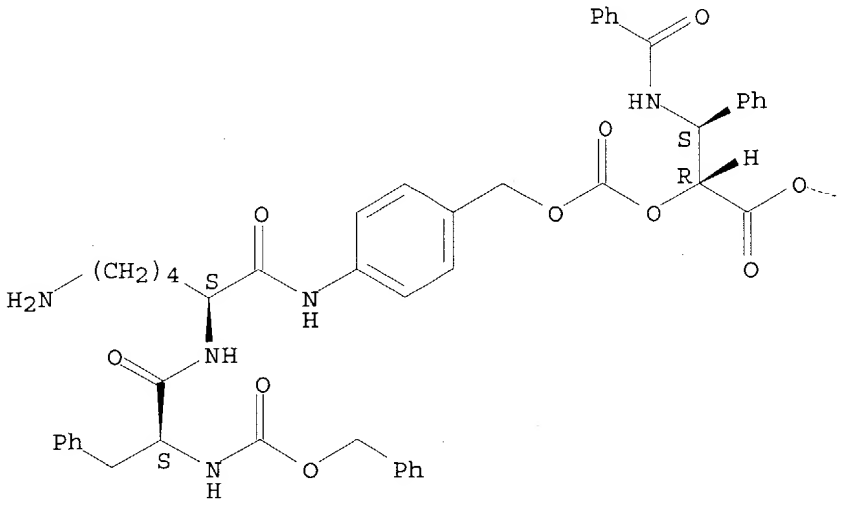
9-yl]oxy]-1-[(S)-(benzoylamino)phenylmethyl]-2-oxoethoxy]carbonyl]oxy]methyl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

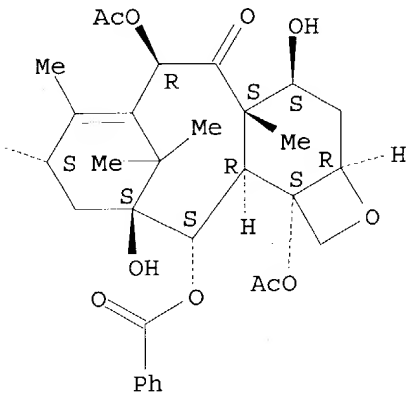
Absolute stereochemistry.

PAGE 1-A



● HCl

PAGE 1-B



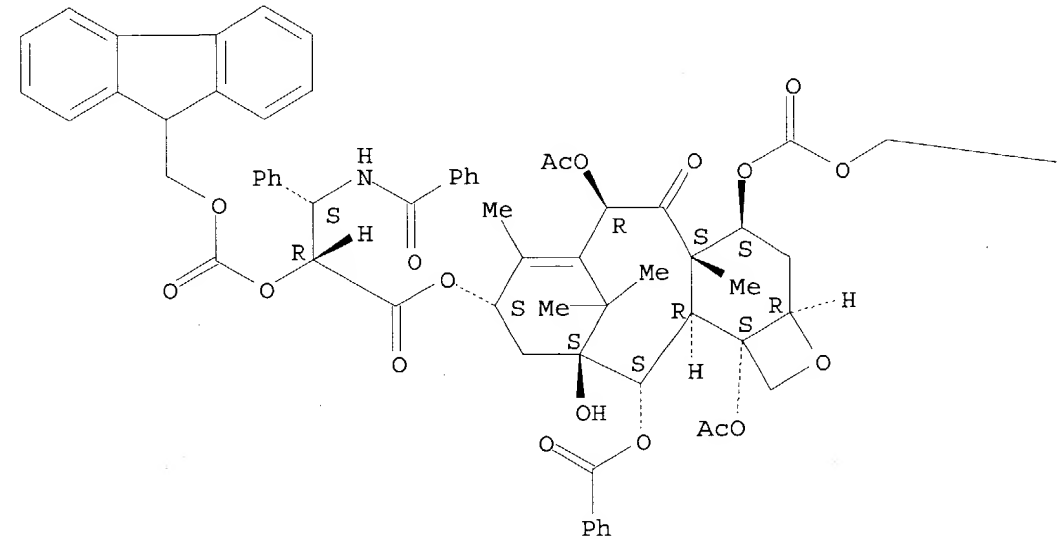
RN 159858-15-8 HCAPLUS

CN L-Lysinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N6-[(9H-fluoren-9-ylmethoxy)carbonyl]-N-[4-[[[[[6,12b-bis(acetyloxy)-9-[3-(benzoylamino)-2-[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]oxy]methyl]phenyl]-,

[2aR-[2aα,4β,4aβ,6β,9α(2R*,3S*),11α,12.alpha.,12aα,12bα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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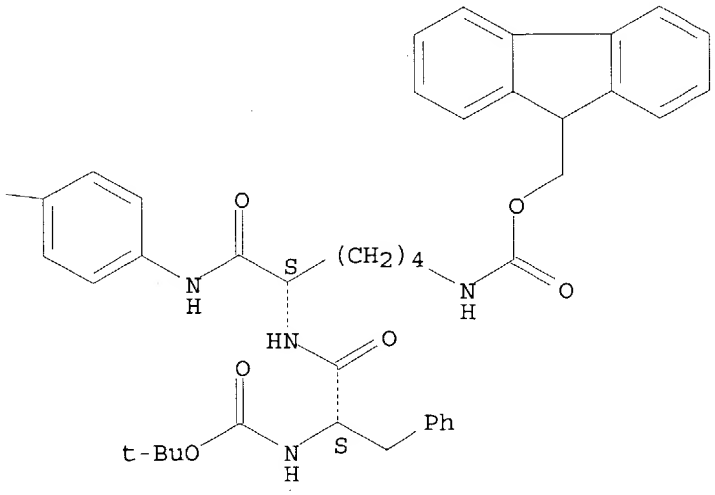


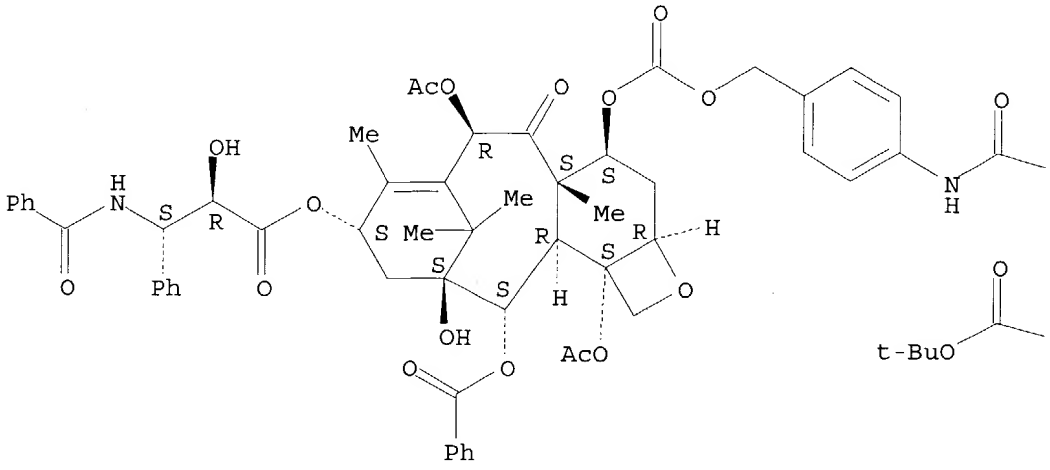
RN 159858-16-9 HCAPLUS

CN L-Lysinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-[[[[[(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-9-[(2R,3S)-3-(benzoylamino)-2-hydroxy-1-oxo-3-phenylpropoxy]-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-4-yl]oxy]carbonyl]oxy]methyl]phenyl]-, monohydrochloride (9CI) (CA INDEX

NAME)

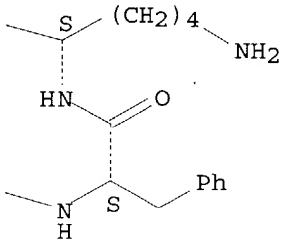
Absolute stereochemistry.

PAGE 1-A



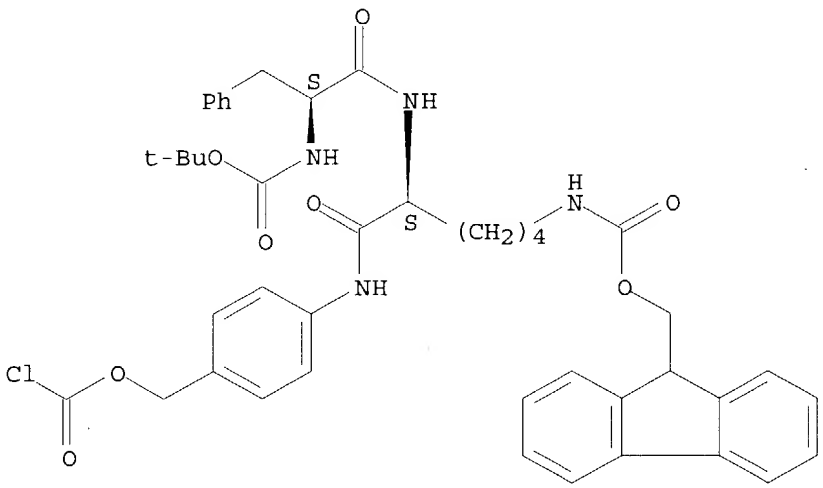
● HCl

PAGE 1-B



RN 159858-17-0 HCAPLUS
CN L-Lysinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-[[(chlorocarbonyl)oxy]methyl]phenyl]-N6-[(9H-fluoren-9-ylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 159858-18-1 HCAPLUS

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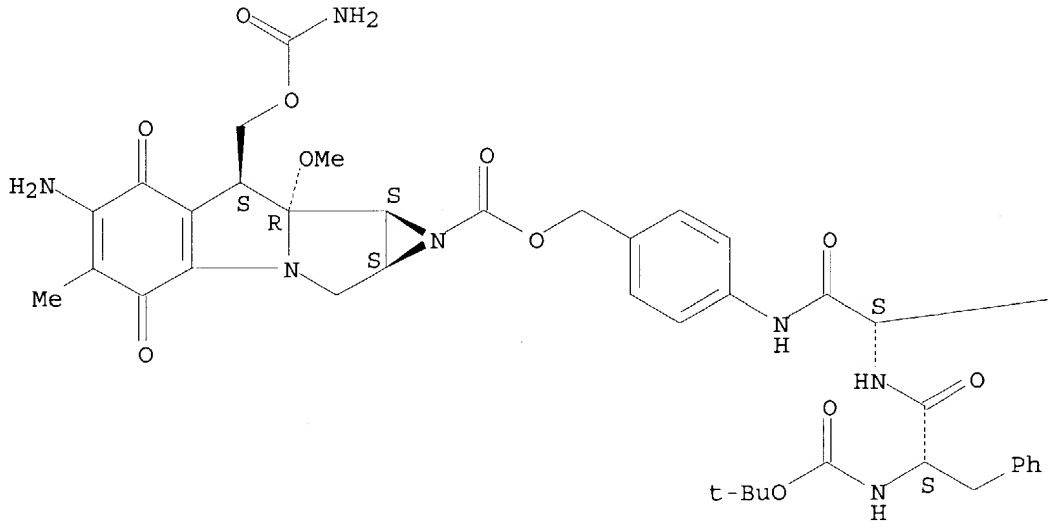
Absolute stereochemistry.

PAGE 1-A



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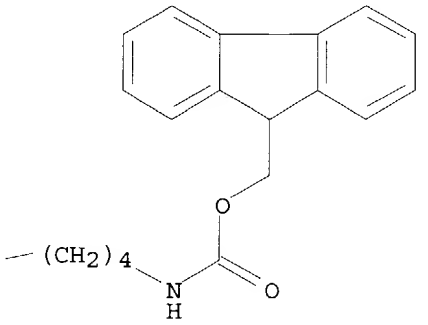

RN 159858-19-2 HCAPLUS
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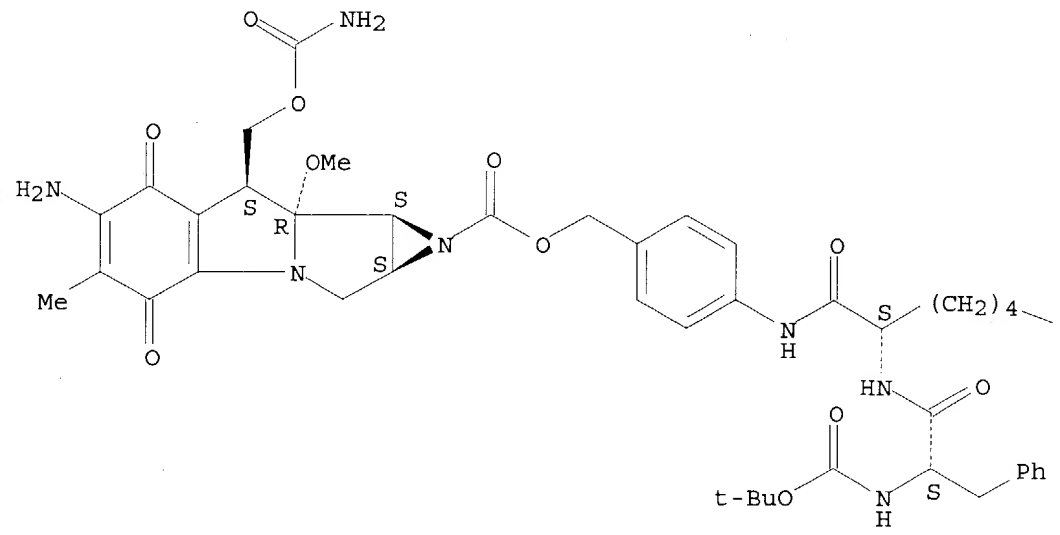
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

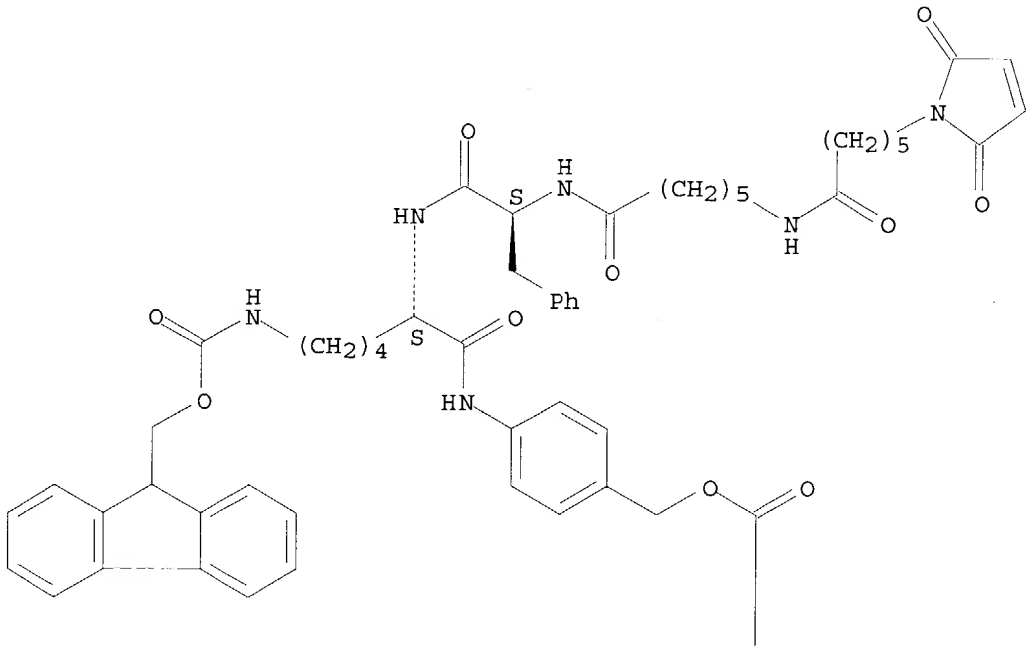
● HCl

NH_2

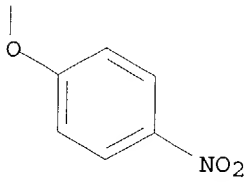
RN 159858-27-2 HCAPLUS
CN L-Lysinamide, N-[6-[[6-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxohexyl]amino]-1-oxohexyl]-L-phenylalanyl-N6-[(9H-fluoren-9-ylmethoxy)carbonyl]-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



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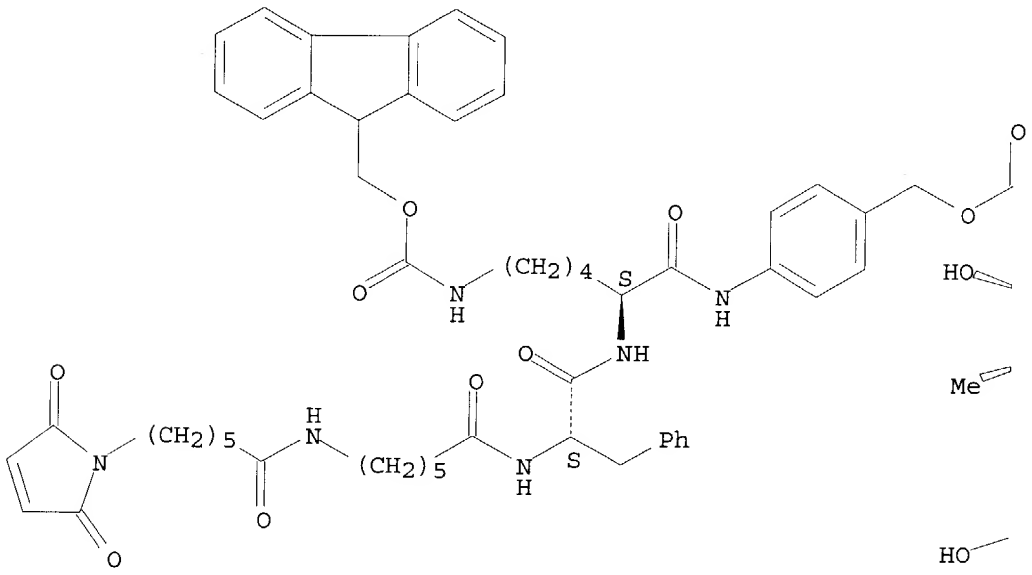
Absolute stereochemistry.

PAGE 1-A



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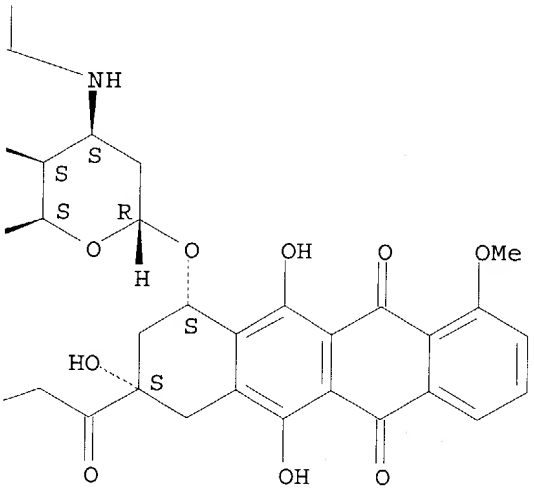

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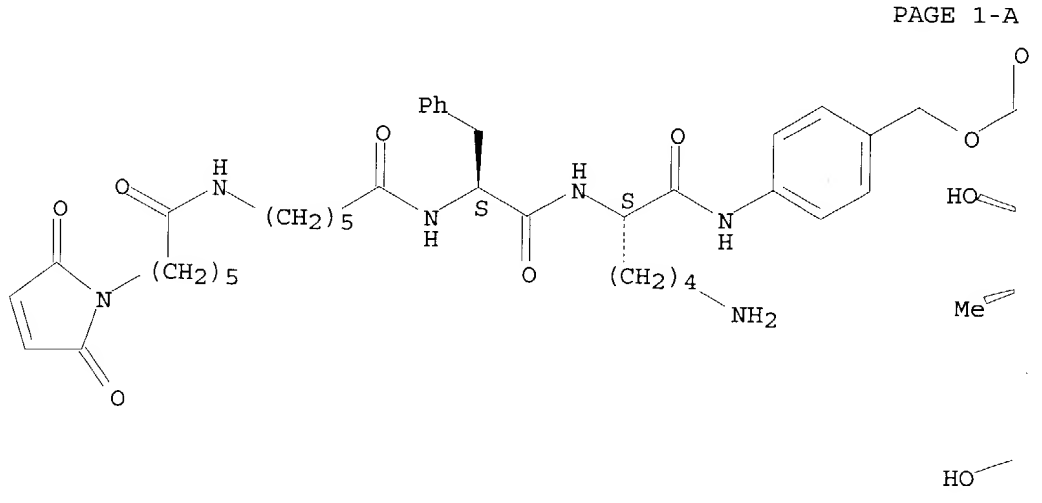
Absolute stereochemistry.

PAGE 1-A



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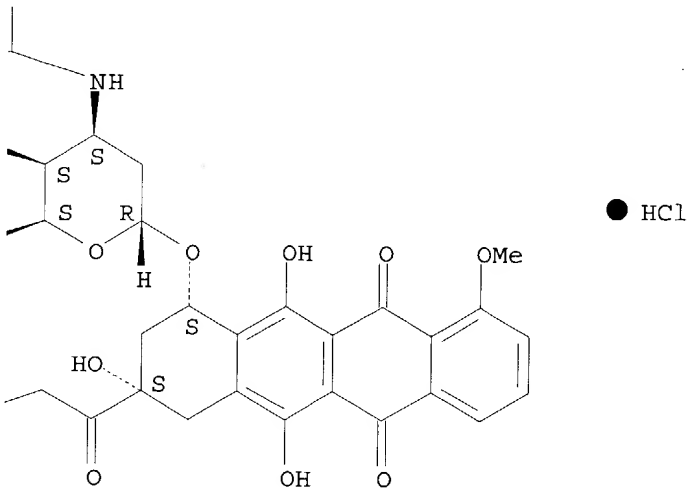

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	230.70

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-8.32

SESSION WILL BE HELD FOR 60 MINUTES
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